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Part I.—Original Articles

"PSYCHIATRY LTD."*

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I AM satisfied one of the results, if not the objective, of medical education is for doctors to judge their success, or the state of progress of any branch of medicine, against a pathological rather than a sociological criterion. This is the inevitable effect of the amount of time and attention given to pathology in the medical curriculum, and is further reinforced by what is asked in examinations.

Traditionally, the problem for the doctor is to try to determine the pathological lesion, using this term at best in a wide sense, and to control this if he can; and the pathological criterion of disease he has in mind is an objective physical criterion, demonstrable in life or after death.

As we all know, no pathological lesion in this traditional sense is demonstrable in a large number of patients who go, or are brought, to see doctors. All physical examinations and investigations prove negative. Medicine is therefore faced with the dilemma in these cases of either (a) coming to the conclusion that there is nothing wrong, which is often clearly untenable, or (b) of expanding its scope almost indefinitely to cover every type of maladjustment.

What I am mainly concerned with in this address is where it may be prudent to call a halt in an expansionist campaign, with special reference to psychiatry.

Expansionist claims are widespread and have authoritarian backing. For example, Dr. Brock Chisholm, Director-General of the World Health Organization, has written: "Perhaps there has never been in all history a more authoritative definition of any word than that provided for the title of this chapter." (It is entitled "Health.") "In a historic document, The Constitution of the World Health Organization, sixty-four nations have decided just what the word 'health' meant. The first statement of principle in that Constitution is the definition of health in these uncompromising terms: 'Health is a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity.' Here (adds Dr. Brock Chisholm) is one word concerning the exact meaning of which dictionaries will not have to worry from now on."

The worrying thing about this definition of health to doctors, if not to dictionaries, is that the logical implication of not being healthy is that you are ill; and it would be a poor psychologist who did not realize that the average man in the street believes that if he is ill he needs treatment, and moreover, that he equates illness with irresponsibility or at least diminished responsibility, and since nobody is in a "state of complete physical, mental and social well-being," everybody is sick.

Dr. Brock Chisholm goes further. He writes of "The acute need of the modern world that modern psychological medicine shall expand its goals beyond the mere helping of individuals. . . . Practitioners of psychological medicine must now advance much further into the preventive field and concern themselves with positive mental and social health, which means that their chief concern should now become the prevention of mental and social disability rather than just its treatment." Later in the same chapter he writes: "Natu-

* The Presidential Address to the Section of Psychiatry, The Royal Society of Medicine, delivered on the 9th October, 1951.

rally parents, educators, youth workers, social workers, politicians and many others have very important responsibilities, but the technical guidance can come only from the students of human mental and emotional development and function"—or in brief, from psychiatrists. In psychiatry, too, you will not be surprised to hear, lies the best hope of resolving international tensions and so preventing war. The great need is that everybody should reach "emotional maturity free from neurotic drives." How this desirable objective is to be brought about is only sketched in outline, but "amongst factors that commonly tend to slow, to distort and to prevent satisfactory social development" Dr. Brock Chisholm lists: "6. Teaching children to believe in the reality of fantasies such as fairies and Santa Claus . . ."

You may recall that in "The Importance of being Earnest" Gwendolen says to Cecily: "On an occasion of this kind it becomes more than a moral duty to speak one's mind. It becomes a pleasure." And Cecily replies: "This is no time for wearing the shallow mask of manners. When I see a spade I call it a spade." Fortified by this precedent, when I see bosh I call it bosh.

It will be observed that according to the Director-General of the World Health Organization—and he is not alone—the proper sphere of psychiatry is very wide indeed and extends far beyond the mere helping of individuals; it would seem to involve world reform. All this is put forward, not as a vague aspiration for the future, but as something to which the "technical guidance" of psychiatry can and should be applied now.

How then are these vast claims to be justified and on what is this technical guidance to be based? It seems to me that the clue to the answer is sought and given in terms of psychopathology of an analytic type. Excluding the bigger questions of international tensions and the like and turning to the mere individual, neither patients nor doctors are likely long to be content with the bare assurance that a departure from complete physical, mental and social well-being spells sickness; they will want to know the cause—the pathology; and when no pathological lesion in the traditional sense is forthcoming, the cause or pathology is sought and found in terms of psychopathology.

Now as I see it, the difficulties about psychopathology as a cause and criterion of sickness are: (1) psychopathology is not objectively demonstrable; and if objection is taken to this statement, it is at least true to say that it is not objectively demonstrable in the same way as traditional pathology; and (2) in the "psychopathological" there is much that is not abnormal. No clearly cut dividing lines can, of course, be drawn between the normal and abnormal in many fields; but with psychopathology the dividing line from allegedly normal psychology seems to be particularly fuzzy. For example, I have served on committees concerned with medical education in psychiatry. It is usually advocated in such committees that medical students should receive instruction in normal psychology in their pre-clinical period. Leaving aside the distressing differences that are apparent as to what this instruction should be, it has been my experience that my more analytically minded confrères have advocated instruction in what they claim to be the normal phases of sexual development in childhood, more or less directly derived from Freud. If, in fact, the Oedipus situation is a normal phase of development, the persistence of a mother-fixation becomes less convincing as an explanation and excuse for anti-social behaviour in later life; and if the criterion for abnormality is quantitative, how is this to be measured, except in terms of the anti-social behaviour itself?

You may think this mother-fixation example an extravagant one, but I have met with it and in circumstances that were irritating at the time. I am sure many of you could cap it with others, as I could too. The case I have in mind was a naval officer recalled early in the war who soon got into disciplinary difficulties from drinking too much. Invaliding and exculpation were advocated by a psychiatrist (not a naval psychiatrist), on mother-fixation grounds, and a report of this kind took some explaining away to the surgeon rear-admiral, who regarded it as just the sort of nonsense psychiatrists are apt to think and to write. "There would be no end to it if this went through" was what he said with the best, but firm, service manners.

I submit that just as general physicians and surgeons tend to be too exclusively concerned with pathological questions (hence "social medicine"?), so psychiatrists tend to be too exclusively concerned with psychopathological questions. The

dangers of the latter preoccupation are greater; for whereas the demonstration of a pathological lesion in the traditional sense is, on the whole, good evidence of disease, the demonstration of a psychopathology is not necessarily so, unless we wish to extend the term "disease" to include everybody; for in a sense we all have a psychopathology.

I would further submit that this preoccupation with psychopathological criteria, rather than, as I would wish to see, with clinical and prognostic criteria, is one of the reasons why psychiatric claims have got out of hand. It is not easy to prove or disprove a psychopathological interpretation, whereas a prognosis can be shown much more readily to be right or wrong.

CRIME AND CRIMINAL RESPONSIBILITY.

Some of the points and the difficulties I have in mind may be illustrated by medical and psychiatric claims in the fields of crime and criminal responsibility.

I think, in general, medical claims are as follows. The first claim seems an eminently reasonable one, namely that the sick should be regarded as medical responsibilities. The second is that sickness implies irresponsibility, or at least diminished responsibility. And the third claim is that the criterion of sickness is the demonstration of a pathology.

I have been involved in two murder cases that showed, as I thought very strikingly, how deeply rooted these conceptions are in medical thought. The first case had a typically epileptic spike and wave E.E.G., and the second an E.E.G. which was suggestive of a localized brain lesion. The first man had no history of epileptic fits, and his crimes disclosed very clearly a capacity for rapid adaptation to altering circumstances and other features that were not consistent with epileptic confusion or automatism; whereas the second man showed no organic mental changes and at the autopsy no evidence of a cerebral lesion was found. Nevertheless it was argued, with considerable feeling, that the demonstration in both cases of a "brain pathology" should have modified the operation of the law, which was the death sentence; in fact both men were hanged.

Now I am not concerned here as to whether the death penalty should or should not be abolished; personally I think I would like to see it go. Consider the practical consequences if the discovery of pathological findings such as these men showed, which could not be directly related to their criminal acts, necessarily conferred immunity from the legal consequence of crime. That this happened to be the death penalty in these two cases is irrelevant. For if immunity is conferred, preventive steps should be taken—in the same way that epileptics are now prevented from holding a driving licence. Could it seriously be proposed that the possessors of an abnormal E.E.G. should be prevented from entering into business contracts or partnerships or in other ways be deprived of their civil rights? If we did not do this, would we not be making the possession of an abnormal E.E.G. a criminal asset?

Thus, the question of criminal responsibility raises many difficulties even when there is a pathology for which objective evidence can be offered. The difficulties are greater in those cases where no organic pathology is demonstrable. It may be recalled that according to the World Health Organization definition of health—"positive health"—all criminals lacking, as they must, complete social well-being are necessarily sick. Crime, according to this view, must be a manifestation of disease, and the treatment of disease, so the argument runs, is a job for the doctor. Further, since we all have a psychopathology, this can always be adduced to back up the thesis that the criminal is a sick man, as in the case of the naval officer whom it was claimed was suffering from a mother-fixation.

I fear that comparable psychiatric evidence is too commonly given in the courts, as any barrister will be pleased to tell you, and I believe it does psychiatry a lot of harm; for the judiciary echo my surgeon rear-admiral's "There will no end to it if this goes through."

WORKING CAPACITY.

Expansionist dangers can also, I think, be seen in connection with the assessment of working capacity. For example, in so far as the doctrine of positive health spreads, inefficiency, like crime, is necessarily rather than possibly a medical

problem, and, in so far as this is accepted, the medical profession, and in particular psychiatry, will increasingly be asked to shoulder burdens I think they will be wise to repudiate.

The first illustration I have in mind shows how this is happening already. I would submit as a basic point that a man's efficiency must be assessed by his employer, his state of health by his doctor. I think it is absurd to suppose an inefficient man is necessarily sick. We all know, however, that in Government Departments, for example, it is extremely difficult to be sacked for inefficiency on executive grounds. Inefficients and ineffectives are consequently referred for medical disposal, but of course far more common is the problem of the man who claims he is unfit for work or for duty. It was a problem met with repeatedly in the services in the war, and is one still very much with us.

I think we should firmly face the obvious and make a stand. I am not suggesting that the decision should be taken lightly or without careful investigation, but I think we can and should say, when the occasion arises, that we can find no evidence of disease, or any reason why the man should be discharged on medical grounds (even if he is inefficient), or any medical reason why he should not work as the case may be.

The sensible view is surely that many individuals present social rather than medical problems, as in the case of the work-shy; and for these people responsibility should be shouldered by society rather than by medicine. In addition, there is a group of betwixt and between, such as certain psychopaths, where responsibility should be shouldered by both, and not by doctors alone. Is there not a real danger of falling into the fallacy that because a problem has psychiatric implications or aspects it should be regarded as a purely psychiatric affair? Apart from our ignorance as to what we could do, I do not see how many of these para-medical or para-psychiatric problems could be tackled without resort to compulsory powers; and since the exercise of compulsory powers interferes with the liberty of the subject, they should only be sanctioned by society as a whole, if sanctioned at all. In brief, as I see it, we should be reasonably strict in our standards as to what constitutes sickness and our job. The concept of positive health is either meaningless or has—as a recent government publication said in another connection—"unacceptable implications." Down with it! *Ecrasez l'infâme!*

PSYCHOTHERAPY.

A "practical art" such as medicine may be judged by what it can do. What can we claim to do? Psychiatric treatment is not of course synonymous with analytic psychotherapy; and this is no place to discuss the value of psychiatric treatment as a whole. As mentioned previously, if you are told or believe you are sick, you expect to be treated; and increasing numbers expect to be treated by some lengthy form of psychotherapy or analysis. I believe quite unjustified expectations have got about. The following is a case in point: The patient "Elmer," an American, was brought reluctantly to my out-patients at St. George's by his girl friend. She at once explained to me that she was not his wife; that as a member of the communist party it was against her principles to be married, but she had a child by him. She was clad in what looked to the male eye like warp and woof and was shod in sandals. She had been a student at the London School of Economics. She said she had brought Elmer to see me since obviously he needed analysis. There must, she thought, be some fixation, since he seemed to lack literary inspiration and what he wrote was banal. It was curious, she added, since sexually he was quite potent.

Elmer, who must have been at least twenty years older than she was, had thick white (American) hair and looked like a bogus and embarrassed senator. It turned out that he had not worked for many years but had led a reasonably successful and not unhappy life living with and on various women. The price he had to pay for his latest venture (being an "artist" had always been his line) was to be placed in front of a typewriter each morning and urged to release his pent-up inspirations, but he found he had nothing to say. The allowance given to his girl friend by her parents had satisfied his material wants.

You will not be surprised that my attempted explanation to the girl that not everybody was born with creative literary gifts that could and should be released by psycho-analysis was countered by the questions: Did I not believe in psycho-

analysis? Did I not believe in psychotherapy? If in fact Elmer had not creative literary gifts, what would I advise him to do? There must surely be something he was best suited for? What about vocational guidance? What treatment would I prescribe?

Ever since I can remember, or rather ever since I began to take an embryonic interest in psychological and psychiatric matters as an undergraduate at Cambridge, I have read repeatedly of the vistas opened by the light shed through the discoveries of Freud, of how psychology and psychiatry had become "dynamic," and of how treatment by psychotherapy had been revolutionized. One of the results of these repeated claims has been, I think, that the girl friend's psychotherapeutic hopes for Elmer are only an extreme example of widely held views, namely the belief that psychotherapy *should* be able to transform an individual's personality, and that there are no limits to people's potentialities when freed from the emotional ties and entanglements rooted in their childhood. The buried treasure school of psychopathology, the faith in the hidden complex which if unearthed leads to cure—or even transformation—is far from being dead and gone and is very much alive and kicking. Indeed I think that with only slight modification this is a view commonly held on psychiatry and psychotherapy, not only by the man in the street, but also by many of our medical colleagues as well.

No one I think doubts that psychotherapy can be of real value, but what are the claims that can be made for analytic psychotherapy? As I see it, and as the majority of psychiatrists with whom I have worked or discussed the matter have seen it, prolonged psychotherapy or analysis is only called for, and is certainly only practicable, in a small minority of cases. I think we should say so, and say it loud and clear, for it is a quite different view to that which has so long been shouted in the public ear.

The position is that, happily, a very large number of patients get better without analysis, either with the aid of simpler measures—or other measures—or with no specialized aid at all. (When I once wrote a small paper mentioning this point I was, strangely enough, accused of pessimism.) There is another large group in which I believe the only sensible possibility is to try to get the patients to accept their limitations, with no hope of making them new men. I believe it is thoroughly bad mental hygiene and thoroughly bad psychotherapy to encourage the public or the patient to expect the probability of a transformation scene from psychotherapy or analysis. Indeed, the sad fact is that after all these years a convincing case for the special efficacy of analysis as opposed to other or simpler procedures has not been made out, or if it has I should like to know where. At the same time I personally believe that, although the majority of cases do not need it or do not benefit from it, a case for prolonged psychotherapy or analysis does exist in a small group—perhaps 3 per cent. of those seen by someone like myself. Treatment by psychotherapy is certainly more widely available; this is an advance; but are the results achieved by psychotherapy of any kind any better than they were thirty or forty or more years ago? The results seem to me to depend so largely upon individual gifts, irrespective of schools and, within limits, irrespective of the procedures adopted, that I doubt it. Did Freud, for example, get better results than Forel? Who now can claim better results than either? Is not the answer that we do not know?

I would submit that the reason for this astonishing state of affairs, namely that we still are waiting for evidence as to the special efficacy of analysis as a method of treatment, lies in the direction of interest of the analysts. This often does not seem to be clinical or prognostic so much as concerned solely with the psychopathology. I have tried to read some of the literature and I am sure many others have had the same experience as I have, namely that whilst interpretations abound, it is remarkably difficult or quite impossible to determine what was the patient's condition before, during or after treatment.

It is surely reasonable to want to know what were the disabilities the patient showed and whether the treatment did good and what good it did, in addition to interpretations of the dynamics of the situation in psychopathological terms. For example, in a recent discussion on the treatment of obsessional states at this Society, the two opening speakers gave no data about the results of treatment at all, but were exclusively concerned with psychopathological theories and problems. This would have been fair enough if the subject for discussion had been the psychopathology of obsessional states; but it was not.

I think these preoccupations with psychopathological rather than with clinical problems must be the explanation why publications concerning the results of psychotherapy should be so few in number and uninformative practically.

What then is the remedy? I know that to advocate a clinical approach is apt to be regarded as a reactionary desire to return to the bad old days of descriptive psychiatry before our subject had become "dynamic" (a word that deserves to be paid over-time). I can however see no objection to it and many advantages; and clinical psychiatry can be combined with a certain modicum of human understanding.

The main clinical problems are diagnostic, prognostic and therapeutic, and the three are of course intimately connected. Clinical studies are necessary for their solution. Who can doubt, for example, our ignorance of the natural history of many disease groups or the unsatisfactory state of many of our present clinical groupings? To illustrate the first, or natural history problem, I have been struck by the fact that the majority of the severe obsessional states I have seen have been in the twenties or early thirties. I have seen fewer in the forties and fewer still in the fifties. What happens to severe obsessional states as they get older? I have asked a number of experienced psychiatrists, and after humming and hawing they have in the end come clean and confessed that they did not really know.

The difficulties of clinical studies are obvious; they flow inevitably from the nature of psychiatric disturbances, for however these may be mediated, they are manifest in disturbances of social effectiveness and social relationships. They cannot therefore be judged without taking social criteria into account. I cannot share the view that the lack of an objective criterion, such as may be said to obtain in traditional pathological studies, make the difficulties insuperable; and as you will have gathered, I do not believe that pathology can be replaced by psychopathology for purposes of assessment; the analogy is false. In any case, social questions can only be answered in social terms. I believe that the questions as to how the patient feels, what can he do and what do others think of him, lend themselves to more definite answers than can be described intelligibly.

Still, if we do not know as much about prognosis and treatment as we should like to know, the knowledge that is available is not inconsiderable.

SELECTION.

When anything goes there can be no limit to that expansionism in psychiatry which I feel to be so injudicious. I have tried to convey something of the undesirable implications of psychiatric attempts at dominance in the social fields of politics, criminal responsibility, and employment—attempts that seem buttressed by a false analogy between psychopathology and pathology, and are promoted by a sales technique that leads the public to unwarranted expectations of what we can give. I should like, however, to touch on just one more expansionist field, namely that often referred to as personnel selection.

There can of course be no doubt about the desirability of placing people in jobs best suited to their desire and capacity, even if there is a danger of this becoming regarded as a right. The last war showed a remarkable expansion in psychiatric selection, both in claims and in practice. But are we wise, as psychiatrists, to stake our claims as regards positive selection? By which I mean, for example, the selection of good officers rather than the exclusion of those likely to break down?

It seems to me that the difficulties in positive selection have been glossed over with special reference to (a) what we can claim to do and especially what we can claim to do in our *professional capacity*, and (b) professional confidence.

(a) The traditional medical role in selection has been one of exclusion. It has not, in the past, been the doctor's job to choose the football eleven, but merely to express his opinion as to whether a man was or was not fit to play. It is true that if a doctor happened to be an expert on football he might be elected a member of the selection committee, and he might even be the most valuable member of it; but he would not have been chosen a member of the selection committee because he was a doctor.

It is important to distinguish what we are doing in our professional capacity and what we are not so doing. Now I might be able to choose officers better than Brigadier Blimp; but if I could; I think it would be mistaken for me to suppose that this resulted from my psychiatric training and was another feather in psychiatry's cap.

On the other hand, a psychiatrist can claim that as the result of his professional training he is better able to predict men likely to be unstable and to break down than those who have not had this training; and further, that as a result of his specialized skill he is better able to assess the type and severity of a breakdown if this occurs. At least I hope he can make these claims, although I must add at once that the prediction of breakdown is a remarkably difficult task.

I believe psychiatry would do well to try to become more skilled at negative selection, which is its job, before embarking upon more ambitious projects, which I submit are not.

(b) The other objection to positive selection is that of professional confidence. It seems to me that the type of difficulty about to be outlined must have occurred in any co-operative selection procedure such as the W.O.S.B's of the war; but I have not seen it mentioned. Executive bodies are unlikely, and I think that would be unwise, to leave positive selection solely to psychiatrists; but in any co-operative selection procedure the problem of a breach of professional confidence must surely arise. For in order to assess a case adequately, a private interview is essential; and in a private interview, matters may readily emerge that it would be a breach of professional confidence to disclose.

This is no theoretical danger or possibility, as the following illustration will show. Shortly after being demobilized I was asked to see cases for the Civil Service Commissioners. So far as I could ascertain they did not have a psychiatrist, nor indeed any medical man on their selection board; but they proposed to refer cases they considered doubtful as regards stability. Almost at once a candidate, whom I saw privately, told me about certain intimate details of past difficulties when I was going through his work record. I am sure he would only have disclosed them confidentially to a doctor; he was no fool. I wrote a report stating, rightly or wrongly, that I could find no medical reason why this candidate should not be accepted. A long correspondence with the Civil Service Commissioners ensued. I was asked to amplify and give full details of what had come out. This naturally I refused to do; and perhaps equally naturally the Civil Service Commissioners have not employed me since.

Now it seems to me obvious that if I had warned the candidate, like a police officer, that anything he said might be used in evidence against him, he would not have spoken freely. This would surely have handicapped me in forming an adequate opinion. Whereas if I had not warned him, and then conveyed to the Civil Service Commissioners what he told me, I would have been guilty of a gross breach of professional confidence.

I would submit that, quite apart from the questions of the capacity and qualification of the psychiatrist to contribute to positive selection, this question of professional confidence will, or should, permanently limit our contribution to positive selection procedures. I believe reasonable lay people (amongst whom, for obvious reasons, I would not include the Civil Service Commissioners) would be less likely to complain of lack of co-operation if they understood this point, which is not, I should have thought, a difficult one to appreciate.

I conceive it possible—in fact I know very well—that some will regard what I have said as merely destructive. I would not agree; but I think I should end on a more obviously constructive note. I am not arguing that we should be like an assembly of filleted civil servants, with “pass to you” as our pass word.

The practical point is what can we do; and if I draw largely on illustrations from my own hospital, this is because I know this best. Our allotments differ; mine happen to lie in a teaching hospital; and everyone knows that teaching hospitals in this country have no reason to be superior or up stage so far as psychiatry is concerned. An inspiring example of what can be achieved in psychiatry was evident to all who attended this year's meeting of the R.M.P.A. and saw something of the work of the Crichton Royal, Dumfries.

But before turning to more parochial problems, I should like to touch upon a general issue. It has been suggested to me by a friend that having attacked the analysts for their restricted approach to aetiology, an alternative theory of causation in psychiatry should be proposed.

As a staunch Meyerian one sees the cause of “functional” mental disorders in an ensemble of factors. Causation, in other words, is a process; and to incriminate a single factor within this process is often to misrepresent its character. At the same time, one factor—sometimes more than one—may exert a specific effect

within this process which others do not. Thus the available evidence suggests that a gene is the specific one among the factors associated with schizophrenia; and if the analysts could demonstrate specific psychopathological factors in mental illness they would be on strong ground. In fact the "lesions" they find seem to be quite unspecific and are rarely proved even to be relevant. Unsolved conflicts that can be discovered in people who are quite healthy by any reasonable standard are blamed, when found in patients, as the cause of schizophrenia, obsessional neurosis and depression; or so it seems to me.

To return, so to speak, to my parish mission; owing to the widespread incidence by far the major part of psychiatric work will necessarily always be tackled by those who are not psychiatrists. Adequate instruction of the doctor-to-be is therefore of fundamental importance, and constitutes—potentially—one of the most constructive contributions to psychiatry that can be made. Nor must we forget nurses. It is therefore essential, quite apart from the urgent demands for treatment, for all teaching hospitals to have a reasonably large psychiatric out-patient department supplemented by in-patient beds.

At St. George's the Board of Governors have taken an enlightened view of psychiatry. We have for example been given facilities that permit of some 65 "doctor sessions" for out-patients weekly (45 for adults and 20 for children). To show that we do believe in the value of psychotherapy, I find that we refer about 20 per cent. of our new adult cases specifically for this; but the treatment they receive varies enormously, ranging from very few to 50 interviews or more. Under 2 per cent. are seen as often as twice weekly over months. This is not the result of any central directive, for my psychotherapeutic colleagues have naturally complete discretion as to how many patients they take on and how often they see them.

Turning to nurses, a new sister tutor, who is mentally trained, has just been appointed, and it is hoped that as soon as our in-patient unit is expanded we shall have an affiliation scheme for training with a mental hospital group. We have been handicapped, so far, because our in-patient unit had only twenty-eight beds (with an average duration of stay of between five and six weeks), but within two months we should have fifty beds. We should have had these additional beds long ago but, unfortunately for us, the enlarged mortuary accommodation necessitated by the increasing activities of our surgical colleagues obtained building priority.

We none of us, I think, set much store by set lectures, holding that the average medical student learns far more from lecture demonstrations, and above all from taking cases himself, which all must now do. We try to teach history-taking, that "ancient history" is not the only relevant part of history, that the collection of facts must precede their interpretation and also that the obvious is not to be despised. And as regards treatment, we teach that "one way only" is the worst possible slogan for psychiatry.

I think the majority of our students regard psychiatry as mildly interesting, and recently I was encouraged by one of them saying to me I could say quite interesting. Some are really interested and first rate at it; but, as many have said to me, it is of little use in examinations.

The biggest practical step forward for the teaching of undergraduate students in this country would be to have a compulsory examination, as in Edinburgh, or at least one compulsory question in all qualifying examinations. Examinations are the only effective way to make the average student take a subject seriously. Medical students are practical people; they want to get qualified; and they naturally tend to feel that time spent on a subject that has very little value for this is relatively wasted time.

Psychiatry is such a large and important subject that, without claiming it as the other half of medicine, which is absurd, the case for being examined on it is overwhelming. I think the public would be astonished to learn that many and probably most doctors can still qualify without ever having had their knowledge tested on a group of disorders that fill approximately 40 per cent. of all the beds in the country, accounted for 25 per cent. of all invalidings from the services in the last war and—but I need not go on.

Nor is the postgraduate situation any better. Thus in the five years 1946–1950, inclusive, out of 136 questions set in the Membership, only 3 were explicitly psychiatric, and only 7 more could be conceived to have a psychiatric slant; and a very rum collection of questions they are too.

In conclusion, when one looks at the vast fields there unquestionably are in the domain of psychiatry and at how much still remains to be done, is it necessary, is it wise, and may it not be rather premature to look for fresh fields to conquer or to fail in? I am told that a Jesuit when visiting a Benedictine Abbey related how he had been vouchsafed a vision. "We don't see visions at Downside" replied the Abbot, who evidently lacked what Dr. Brock Chisholm would call vision. I think I lack vision too. I have no yearning to run the world, and I can say with no false modesty I do not believe I could. My own job is quite enough for me.

I have called this address "Psychiatry Limited." I understand that a limited liability company is one in which the shareholders, should the company fail or go bankrupt, are not liable for more than they subscribe. The company I have in mind is a respectable company, a large concern with big responsibilities and with a great future before it. The shareholders are quiet, diffident, modest sober men who have a real pride in their business, but they are vexed when others undermine the reputation of the firm by using the name to float bogus companies, with grandiose prospectuses, backed up by balance-sheets that do not add up to make sense.

THE PATIENTS' ATTITUDES TO LEUCOTOMY AND ITS EFFECTS.*

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[Received 29 January, 1952.]

It is perhaps not surprising that there have been no studies on the leucotomized patients' attitudes to the operation and its effects. There has been no practical reason for giving that problem special attention. Leucotomized patients have not spontaneously voiced complaints about the operation, even when the result was unsatisfactory. It seems that their apparent silence has been taken so much for granted that psychiatrists have failed to realize that it is an astonishing phenomenon. Here is a group of patients who have been subjected to an operation of which the pros and cons have been widely discussed in public. Many have left hospital free from symptoms but socially handicapped by the side-effects of the operation. Yet there has been, as far as this writer is aware, no instance of litigation in connection with the surgical treatment of mental illness. Part of the explanation for what seems to be a collective indifference to, if not general approval of, the operation and its effects may be found in the type of mental disorder for which this treatment has been most frequently applied: among the patients thus treated there have been many schizophrenics who even after the operation remained out of touch with reality, but that explanation does not apply to the numerous patients who were operated on for affective illnesses and neuroses.

How do patients suffering from mental disorder react to surgical interference other than leucotomy? Many, it is true, show a remarkable indifference, especially schizophrenics. From time to time one comes across a paranoid patient who has experienced an operation as an act of hostile interference to which he attributes special significance. In schizophrenics the break in the body surface which an operation usually implies may give rise to delusions concerning the boundaries of the self (Hemphill and Stengel, 1940†). It is also known that in neurotics injury to, and operations on the head, which holds a special position in the body schema, sometimes give rise to morbid preoccupations. In patients who are given to hypochondriacal complaints an operation, however successful it may have been surgically, may become the focus of persistent grievances. Do leucotomized patients show similar reactions? This is one of the problems on which this clinical study may throw some light.

The observations presented in this paper were made in the course of a follow-up study carried out at Graylingwell Hospital, Chichester, where the bulk of the case-material was studied (Stengel, 1950‡), and continued at the Institute of Psychiatry of the University of London. Each patient was questioned by the writer on his or her attitude to the operation and its effects. First it was ascertained whether the patient realized that he had had an operation. Then he was asked what he thought of the operation, whether it had helped him and in what respect, and what other effects the operation had had. Leading questions about the nature of those effects were avoided. The case-material consisted mainly of schizophrenics, including the paranoid reaction types, and affective disorders. There were 66 of the latter, and 140 of the former. There was, in addition, a small group of 18 patients consisting of neurotics, psychopaths, mental defectives and a few organic cases. The total number of patients questioned was therefore

* Based on a paper read at the Annual Meeting of the Royal Medico-Psychological Association at Dumfries on 12 July, 1951.

† This Journal, 86, 1.

‡ This Journal, 96, 633.

224. They had been operated on from one to five years before they were questioned. The case-material followed up was much larger, but in this study only those patients were included who were able to appreciate the questions and to give relevant answers. In all cases the operation had been the standard leucotomy of Freeman and Watts.

DENIAL OF THE OPERATION.

Thirty-one, i.e., over one-seventh of the patients, were not aware that they had had an operation. Ten of them, when told that they had had the operation, seemed to accept this without surprise, but when questioned a few hours later produced the same negative reply. The rest, when told that they had had an operation on the head, denied it more or less emphatically. When the scars on their temples were pointed out to them they produced all sorts of rationalizations. Some said that their heads had been shaved only. Two patients maintained that the scars were due to electrical treatments, of which they had had many before, and some since, the operation. One patient asserted that they were due to shrinking of the skin. The rest insisted on their denial of ever having had an operation on the head, but several among them spontaneously referred to other operations which they had actually had before or since they had entered hospital, such as teeth extractions and hernia operations. Several of the patients said that they had been better for some time, but they were unable to suggest when approximately the improvement had set in. They did not refer to personality changes such as were related by many patients who were aware that they had had an operation (see below). It was impossible to ascertain whether or not those patients had been unaware of the operation from the beginning as they had not been questioned about this before the present investigation; nor was it known what their attitude to surgical treatment had been before the operation.

Twenty-eight of the thirty-one patients who denied having had the operation were schizophrenics of five to twenty years' standing, two were depressives, and one was a mental defective with epileptic fits. Only one of this group, a paranoid schizophrenic, could be classified as improved; the rest had shown no material change, though there had been some improvement of behaviour in most of them. The schizophrenics showed varying degrees of personality deterioration with marked thought disorder and delusions and hallucinations; their symptoms had remained unaffected by the operation. Their average age did not differ from that of the rest of the patients. All clinical sub-types of schizophrenia were represented in this group. There was no indication that in these patients the operation had been followed by prolonged states of clouded consciousness.

Memory impairment could not be regarded as responsible for the denial of the operation. Only in two of the thirty-one cases was there a memory disorder; the one was a 65-years-old chronic depressive patient with dementia, and the other was the imbecile epileptic. In none of the other patients were there signs of memory impairment. The denial of the operation could not be attributed to negativism. These patients were no less ready than the others to talk about themselves and to answer questions. Body image disturbances were not more frequent among them than among the rest. In fact, they did not show any feature which did not occur also among the rest of the patients. Most of the patients who denied having had the operation were euphoric, but it could not be definitely established that euphoria was comparatively more frequent or more prominent among them than among the others. Nor was it possible to relate that feature to the site of the cuts through the frontal lobes.

THE PATIENTS' SELF-OBSERVATIONS ON THE EFFECTS OF LEUCOTOMY AND THEIR EVALUATION.

All the patients questioned, with the exception of the group described above, and of those who were unable to give a comprehensible answer, were aware that they had had the operation which they called either "leucotomy" or "an operation on the head" or "an operation on the brain." None of the patients broached the subject of the operation spontaneously. In reviewing the patients' answers it is necessary to distinguish between (a) self-observations on the changes which the operation had brought about and their evaluation, and (b) emotional attitudes

to the operation itself. There was often an unexpected and apparently paradoxical discrepancy between the former and the latter. In this chapter it is proposed to deal with the former only.

Of the 193 patients who were aware of having had the operation, 112 were schizophrenics, including those with paranoid states; 64 had been suffering from affective psychoses, mainly depression. The remaining 17 belonged to the miscellaneous group.

The patients' observations on the effects of the operation could be grouped under three headings: (1) gains; (2) losses; (3) no change. These observations often appeared to be unrelated to the clinical results of the operation as assessed by relatives and doctors.

(1) *Gains*.—Under this heading were listed alleviation or disappearance of symptoms, and personality changes which were described by the patients as improvements on their pre-operative disposition. The changes most commonly referred to were the disappearance or alleviation of the tendency to worry and the reduction of tension and anxiety. "I can take things easy; I can relax; life has become brighter" were frequent observations. Sometimes the same adjective was used for different experiences; e.g., a depressive patient praised the operation for having made him "less conscious" of himself, while a schizophrenic patient who had not lost his hallucinations and delusions said that he had been much better since the operation as it had made him "more conscious" of himself.

(2) *Losses*.—These were changes such as worsening of symptoms, affective loss, disappearance or reduction of sexual desire or potency, lack of energy and efficiency, increased irritability, self-confessed lack of consideration for others, etc. Epileptic fits, which had occurred in about ten per cent. of the patients questioned, have not been included in this category. None of the patients referred to them spontaneously, and when asked about them they did not regard them as a liability. There was in many cases a marked discrepancy between the patients' evaluation of the effects of the operation and that by the relatives and the psychiatrists.

Among the schizophrenics there were 21 who thought that the operation had resulted in losses, but 17 of those had noted gains also.

Of the 64 patients who had been operated on for affective illness, 28 had registered losses, but only 2 of these had failed to observe gains also.

It was remarkable how lucidly and fully many of the patients described their gains and losses. Only three expressed regret and resentment about what they had lost. Two of them had suffered from depression and appeared to have made a complete recovery; the third, whose symptoms had not completely disappeared, resented the loss of initiative and blamed the operation for it. Many of the others related their observations in a matter-of-fact manner as if they did not concern them personally. They seemed to be capable of a surprising degree of detachment, but their awareness of the changes that had taken place, especially of the personality changes, must have been very definite and unequivocal, so precise were their descriptions. This was particularly impressive in those patients whose delusions and hallucinations, together with a degree of thought disorder, had continued unchanged after the operation. The contrast between the acute awareness of the personality changes and the lack of insight into their symptoms was very striking indeed.

The proportion of patients who were aware of losses was much higher among those who had considerably improved or recovered than among the others. Of the 21 schizophrenics who had observed losses, 16 had left hospital in varying states of improvement, which in 5 cases was rated as full remission. Of the 28 depressives who had observed losses, all had left hospital; 23 of them were graded as recovered, 4 improved and one as unchanged. Many of the patients who described their personality changes as losses were regarded by their relatives as perfectly well.

None of the patients who were aware of losses as well as gains attempted to balance—one against the other. Any changes they noted were experienced as isolated phenomena.

The patients' statements on their losses almost invariably lacked an undertone of sadness and regret. They sounded rather like reports by an unbiased observer. The changes were described in terms of conventional values which, however, seemed to have lost their feeling tone. There was nothing nostalgic in the way in which the patients talked about their affective losses.

(3) *No change*.—There were 23 patients, 19 of them schizophrenics and 3 depressives, who denied that there had been any change following the operation. Among them were several who had recovered from their symptoms and showed only slight personality changes.

ATTITUDES TO THE OPERATION.

Three attitudes to their own operation could be distinguished among the patients questioned: (1) A positive attitude, which was one of approval or praise. (2) A negative attitude, expressed in statements such as: the operation was unnecessary; it was unsuccessful; it should not have been done; and, in a few instances, it was harmful. (3) An attitude of doubt or indifference as to whether the operation was a good or a bad thing.

(1) The great majority of the patients when questioned expressed approval or praise of the operation. Among them were many whose condition had not materially changed. All of these patients had, when questioned about the effects of the operation, registered either gains only, or gains as well as losses.

(2) Twenty-two patients, i.e., about one in nine of those able to express an opinion, had a negative attitude to the operation; 15 of them were schizophrenics and 7 depressives. Of the schizophrenics, 4 had left hospital, 2 free from symptoms and socially well adjusted, the other 2 improved; the rest of the 15 schizophrenics had remained in hospital. Only one, who was clinically unchanged, said that the operation had made him worse. Two paranoid schizophrenics regarded the operation as one of the many interferences they had been subjected to. In none of the patients whose attitude to the operation was negative did it occupy a special place among his paranoid preoccupations. In none of them had it become the nucleus of a delusion or the source of persistent spontaneous complaints. The majority of the patients whose attitude to the operation was negative thought that it had been unnecessary or unsuccessful.

The patients' attitudes to the operation did not always correspond with their observations on its effects. Two of the depressive patients who had registered gains as the result of the operation nevertheless felt that it need not have been undertaken. They implied that they would have improved without it. All the depressives with negative attitude to the operation had left hospital. In these patients, that attitude was part of their general hypochondriacal outlook. The operation was to them only one of the many, mostly trivial incidents which they groused about when questioned, but never spontaneously. It never figured as an important experience.

(3) An attitude of doubt or indifference concerning the operation was found in 19 patients. Three of them were depressives, one was the mental defective with epileptic fits, and the rest were schizophrenics. In this group there was a closer correspondence between the patients' attitude to the operation and their observations on the effects of the operation than in the other two groups: 15 out of the 19 patients had stated that the operation had made no difference to their condition, while 4 had observed losses only. On the other hand, these self-observations were in the majority of cases at variance with the clinical assessment. Only 5 of the 19 patients had remained clinically unchanged, 5 had made a complete recovery and the rest showed varying degrees of improvement.

In the small miscellaneous group the first and the third attitude to the operation were found, but this group was too heterogeneous to justify a closer analysis.

Most patients who had remained in hospital and some who had been discharged were questioned more than once. Their observations on the effects of the operation and their attitudes to it were both remarkably consistent. There was only one patient whose attitude to the operation showed definite changes. This was a woman who had been operated on for a long-standing obsessional neurosis. After operation she had become subject to periods of severe depression. When she was depressed she blamed the operation for her condition, but as soon as she had recovered from the depression her attitude to the operation, which had almost completely removed her obsessional symptoms, became one of approval.

COMMENTS.

This is no more than a preliminary study of a subject that is worthy of close attention. The present report serves to show the various types of reaction to

the operation that could be observed in a large series. The observations need further elaboration in individual patients.

The changed feeling tone of emotional patterns.—The study of the patients' attitudes to the operation and its effects might be of value for the understanding of their mental reactions in general. The operation is something that has happened to all of them and their reactions to it can be compared. It is a crucial event imposed from outside and initiating a new era in the lives of most patients thus treated. Of this significance of the operation many patients are aware. Yet it hardly stands out from their day-to-day experiences, even where the awareness of the changes attributed to it by the patients themselves is very real and acute. The detachment with which the patients relate their losses is very striking. A change in the feeling tone of emotionally charged experiences has taken place. Whether this is due solely to quantitative changes, i.e., to the reduction of emotional charge, or whether qualitative changes have also taken place it is not possible to state.

The peculiar character of the leucotomized patient's attitude to changes observed by him, especially to those designated here as losses, becomes clearer if one compares it with that of other patients who have become aware of changes in their emotional reactions: such as the young schizophrenic who complains about his emotional impoverishment, or the ageing man who compares his emotional responses with those of his prime. They are obviously able to relate present to past patterns of emotional response and to compare them. It appears that the leucotomized patient is unable to match correctly emotional patterns in this way, possibly because not only the present but also the past patterns of emotional response have lost their appropriate feeling tone. This may be the reason why in the leucotomized patient the awareness of loss is hardly experienced as deprivation although it is described as such, and why it does not engender a real sense of frustration and is not felt as a mental trauma. This may also explain why leucotomy as an experience is hardly ever productive of new symptoms as other operations sometimes are; and why the impact on other persons of the patients' observations of their losses is so different from that of the complaints of patients such as those already mentioned: they lack the tragic character of which one becomes aware when listening to the schizophrenic talking about his emotional impoverishment, or to the ageing man's observations on his waning powers.

The denial of the operation.—A group of patients appeared to be unaware of having had the operation. The reasons for this are far from clear. Had it perhaps not been made plain to them that they were going to have surgical treatment, or had they failed to understand what they were told? This is unlikely to be the explanation. If it were, unawareness of the operation would probably be more frequent than it was found to be; in fact, many of the patients to whom that explanation may apply were aware that they had had the operation. Whether or not patients get to know of operations carried out on them, or of injuries sustained, does not depend only on what they have been told about them before or afterwards. They become aware of those events retrospectively by inquiries and circumstantial evidence. It is true that leucotomized patients often fail to ask questions when they find themselves in bed after the operation, but they usually draw the correct conclusions from the treatment they receive after the operation. Memory disorder or prolonged post-operative clouding of consciousness could be excluded as the causes of the ignorance and denial of the operation. Nearly all the patients belonging to this group were old-standing schizophrenics: advanced autistic withdrawal from reality obviously favours that particular attitude of denial in leucotomized subjects. It was also noteworthy that the majority of the patients who denied having had the operation were not aware of having undergone any change. This may have been another factor contributing to the denial of the operation. However, there were many old schizophrenics unchanged or not greatly improved, who were aware of the operation, and among them some who had not noticed any changes. It cannot, therefore, be assumed that unawareness of changes satisfactorily explains the denial of the operation. Indeed, the denial of that event may tend to inhibit awareness of change.

There is a possibility that damage to certain areas of the cortex, or to certain parts of the fronto-thalamic tracts, may, together with other factors, be responsible for that phenomenon. It is known that the lesions produced by the standard leucotomy vary greatly.

The reactions which these patients display when they are told about the operation are very similar to those seen in patients with anosognosia when they are told the truth about their limbs of whose paralysis or even existence they are unaware. Both either accept the truth for the moment, only to disregard it soon after, or they stubbornly refuse to accept it and resort to rationalizations when called on to explain undeniable facts. This similarity suggests that ignorance of the operation not based on memory loss is a neglect phenomenon akin to anosognosia, and that one is justified in speaking of "unawareness of the operation." Psychopathologically the phenomena are clearly related. The patients who deny the operation are unaware of interference with their physical and mental integrity. It is true that the patient with anosognosia apparently denies an existing disability, while the patient unaware of leucotomy denies a past event, but is this difference a real one? Do not both types of patients deny the advent of change as well as its persistence? Does not the patient with anosognosia deny the loss of motor power as well as its continued absence? And do not certain blind patients deny the actual loss of vision as well as their blindness? It seems that some leucotomized patients deny the event that caused the change as well as the change itself.

Anosognosia and other neglect phenomena occur when a combination of cerebral lesions results in a certain constellation of mental changes. The mood of these patients is almost invariably one of euphoria. In the patients with unawareness of leucotomy euphoria appeared to be more marked than in the others. But this was no more than a clinical impression, which it would be difficult to establish in view of the frequency of euphoria after the operation.

There is still another reason for assuming that unawareness of leucotomy and anosognosia are kindred phenomena. Anosognosia as originally described by Babinski has been found to be associated with thalamic lesions, while in other forms of unawareness of, or indifference to, physical disabilities the frontal lobes were involved, the same parts of the brain, therefore, whose functions are modified by leucotomy.

Unawareness of the operation is not the only neglect phenomenon occurring in leucotomized patients. Many of those with a positive attitude to the operation who were aware only of gains showed marked changes of which they were unaware. Possibly the mechanisms underlying that unawareness were similar to those responsible for the denial of the operation. It is hardly possible to attribute unawareness of personality changes entirely to the desire to overlook unpleasant realities. Leucotomized patients seem to be less subject to that tendency than are others. This is borne out by the free and detached manner in which they speak of their losses and shortcomings. The frequent unawareness of change may be partly attributable to these patients' difficulties in integrating experiences of various kinds and in appraising their total situation in relation to their environment. Isolated experiences are particularly liable to neglect and extinction. Nevertheless, the tendency to repress what is unpleasant cannot have been absent in those patients, otherwise the proportion of patients who had noticed losses would have been much greater. That tendency was obviously less effective where clinical improvement had been greatest: many more were aware of losses among those who had improved greatly or recovered from their symptoms than among the rest.

SUMMARY.

Attitudes to the operation and its effects have been studied in a large series of schizophrenic and depressive patients treated by the standard leucotomy.

A group of patients, about one-seventh of the total, denied having had the operation. When told about it their reactions were similar to those of patients with anosognosia and other neglect phenomena: some accepted the fact temporarily, while others persisted in their denial. That group consisted mainly of advanced schizophrenics. The psychopathological significance and the origin of the denial of operation have been discussed. It has been suggested that gross unawareness of changes following leucotomy is a kindred phenomenon.

The patients' self-observations on the effects of the operation have been registered. Awareness of losses was much more frequent among those recovered or greatly improved than among the rest. The peculiar quality of detachment with which the patients recorded their gains and losses has been discussed. It has been suggested that it is not due solely to quantitative changes, but that, as the result

of the operation, the patients have become unable to match correctly present and past patterns of emotional response as both have lost their feeling tone.

The patients did not spontaneously attempt to balance the losses against the gains.

Three attitudes to the operation have been distinguished—a positive, a negative, and that of doubt and indifference. Often these attitudes did not tally with the self-observations on the effects of the operation.

One in nine of the patients had a negative attitude to the operation which, however, was never expressed spontaneously.

In none of the patients had the operation become the source of a delusional idea or the focus of hypochondriacal preoccupations.

THE LOWER QUADRANT LEUCOTOMY.*

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IN recent years efforts have been made to analyse the part played by the frontal lobes in the integration of personality. The pioneer work of Bianchi (1922) based on pathological lesions in human subjects, and on experimental bilateral ablations in monkeys, dogs and foxes, still appears to be as true to-day as when originally enunciated. Sherrington (1901) also described the changes following destruction of the frontal lobes. It was noted that such animals lost the power to learn and to enjoy themselves. They had no curiosity, but became restless, hyperactive and easily distracted. Brickner (1936) studied over many years a patient with bilateral frontal lobectomy who showed a diminished ability to synthesize abstract thoughts. Goldstein (1941) found that patients with frontal lobe damage lose their power for abstract thought and this is replaced by concrete behaviour, as shown by object grouping tests and their use of words. Similarly Penfield and Hebb (1940), in a case of extensive lobectomy for an infiltrating oligodendroglioma in an intelligent housewife, described a lack of ability for complex planning, such as is necessary for preparing a meal of several courses. Jefferson (1937) was unable to find any deficiency in cases of unilateral lobectomy. Rylander (1939), on the contrary, after lobectomy for tumours was able to detect changes similar to those found by Goldstein, and in cases with frontal lobe injury he found a lack of social sense. These patients were embarrassingly outspoken, and sometimes showed excessive activity or fatigue. Hebb (1945) concluded that studies on pathological lesions of the frontal lobes were not very helpful, owing to the lack of precision of the lesions due to the uncertain extent of the pathology.

All these studies failed to show any precise localization of function, and it began to be felt that the effects of leucotomy were dependent upon the quantity of fibres destroyed rather than their localization. This agrees with Lashley's statistical work (1929) on rats learning to run mazes of different complexity, which showed that it is immaterial as to which primary receiving areas are removed, for the loss of learning power is proportional to the amount of cortex destroyed. The studies of Freeman and Watts together with that of many others, particularly McLardy and Meyer (1949), seem to indicate that interruption of thalamo-cortical fibres is the essential lesion, but it should be stressed that these fibres are a two-way system thought to function by resonance from thalamus to cortex and back again. The exact significance of this is of course unknown.

More recently it has become increasingly appreciated that there is an extensive localization of autonomic function in the frontal lobes. The more this has been studied the more widespread it appears, and it is now known to extend into the temporal lobes and cingulum. Fulton (1951) divides the frontal areas into a lateral and a medial region. The medial region consists of the cingulum, the back part of the base of the frontal lobe, the tip of the temporal lobe and the amygdaloid nucleus. This complex has been called the "visceral brain." In extensive studies on monkeys who have been trained in learning techniques, it has been shown that excision of the lateral region of the frontal lobe upsets their ability to learn, but this is only slightly affected if the lesion is confined to the medial region. To this degree there would appear to be some localization of function in the frontal areas.

* From a paper read at the Northern and Midland Divisional Meeting of the R.M.P.A. held in Sheffield, April, 1951.

It would seem that the mechanism which governs the integration of behaviour is something which is very widespread, and may be located not only in the cortex, but also in the basal ganglia and perhaps even in the brain-stem and medulla. This may be the reason why large areas of brain can be removed without apparently altering the basic personality. In spite of this, and with little or no knowledge of what disorganization has taken place in the brain of a patient with a psychosis, one still hopes by means of a local excision to affect some beneficial change.

It is possible, therefore, that the effect produced by leucotomy or by destruction of the thalamo-cortical fibres depends upon the impairment of resonance in the visceral brain. Recent work on psycho-somatic inter-relationships seems to indicate that this has an important significance in those mental disorders where there is predominance of subjective appreciation of abnormal visceral sensations. In this way quantitative destruction of the fronto-thalamic fibres becomes significant, and if the "cingulum fronto-temporal complex" is the main localization of autonomic representation, then destruction of fibres from these areas will presumably effect a change in these patients, though this may be only one facet of the disturbed workings of their whole brain. No doubt this fibre system can be interrupted with a small destructive lesion placed at some strategical position, dependent upon the facts of anatomy. Our only difficulty is to know exactly where this spot lies. It is this search to obtain the maximum therapeutic effect with a minimal well-placed lesion which is the basis of the numerous different operations designed in the course of the last five years. The very complexity of the clinical material which has been submitted to operation is one reason why recognition of the best operation for the best type of case has been so long in forthcoming. In fact, one is only just beginning to recognize something about what we are trying to accomplish, and how to do it. It is with this object in mind that we have explored the leucotomy question, using the full and the lower quadrant incisions in a parallel series of cases, and we are beginning to feel that it is the deep lower and perhaps central cut which produces the best result without leaving too much frontal lobe deficit. In this operation the upper fibres are preserved, but it is impossible to say in a study such as this which particular areas have been left intact, although these may be revealed ultimately by the studies of Meyer and McLardy. In the meantime, localized excisions may add to our further knowledge of this aspect of the problem.

CASE MATERIAL.

The material under review consists of the first 250 operations of prefrontal leucotomy performed on cases in the Middlewood Mental Hospital. The selection of patients has been largely determined by such factors as long duration of illness, intractability and failure of sustained benefit from other methods of treatment. A constant technique was developed, using either a full or a lower quadrant incision in an almost equal number of cases, the choice being arbitrary at first but finally restricted to lower cuts for depressive states, and full incisions for schizophrenic, manic and psychopathic patients. The full standard leucotomy incision was used exclusively from 1943 until 1946, after which time the lower quadrant operations were commenced (Table I). From this time onward there has been an increased discharge-rate owing to the inclusion of cases with affective disorders, almost to the ultimate exclusion of other types of psychoses.

TABLE I.—250 *Leucotomies*.

Year.	Operations.		Discharges.	
	Full.	Lower.	No.	%.
1943	6	—	2	33
1944	11	—	4	36
1945	6	—	2	33
1946	6	20	11	42
1947	15	13	19	68
1948	21	11	17	53
1949	51	70	79	65
(Part) 1950	5	15	13	65
Totals	121	129	147	59

The distribution of the cases according to age-groups is shown in Table II, together with the discharge-rate. These figures suggest that the chance of a favourable outcome from leucotomy increases with the age of the patient, the discharge-rate reaching a maximum of 76 per cent. in the 51 to 60 age-groups. Relapses, on the other hand, were greatest on the younger 21-30 age-groups, due to the preponderance of the less favourable schizophrenics. It is interesting to note that advanced age could not of itself be considered a contra-indication to leucotomy.

TABLE II.—Age-Groups.

Age.	Operations.		Discharges.		Relapsed. No.	Died. No.
	Full.	Lower.	No.	%.		
11-20 . . .	5	2	1	14	—	—
21-30 . . .	36	22	26	45	9	2
31-40 . . .	38	18	30	54	2	1
41-50 . . .	24	16	27	67	1	1
51-60 . . .	13	33	34	76	3	1
61-70 . . .	3	33	24	66	2	1
71-80 . . .	2	5	5	71	1	1
Totals . . .	121	129	147	59	18	7

TECHNIQUE.

Pre-operatively the patients were given omnopon and scopolamine, and in all but eight cases the operations were carried out under local analgesia. It was felt that any inconvenience arising therefrom would be outweighed by such advantages as avoidance of some anaesthetic complications, the observation of the patient's reactions during brain section, and the desirability of leaving a conscious, actively moving patient at the termination of the operation, thereby facilitating nursing supervision and prompt detection of any post-operative complications.

The operative technique conformed to that of the Freeman-Watts method, using a lateral approach. Burr holes were made 3 cm. behind the outer rim of the orbit, and 6 cm. above the zygoma. The brain fibres were incised by a sweep of the brain cannula after the fashion of McKissock (1943), the section being made just anterior to the plane of the coronal suture. In these operations particular attention was paid to the localization of the sphenoidal ridge, the sweep of the cannula being made just in front of this point, and section of the orbital fibres was verified by feeling the tip of the cannula on the orbital plate. In the lower quadrant operation the cannula was then carried upwards to only 1 cm. above the centre of the burr hole, thereby making sure that the fibres of the central segment were cut. In the full leucotomy the brain cannula was carried upwards towards the vertex.

In the diagram of the operative fields (Fig. 1) it will be seen that the burr holes are positioned at the middle point of the anterior cranial cavity, and that an incision from a level 1 cm. above this point carried down to the orbital plate should incise about two-thirds of the white matter, i.e., rather more than the orthodox lower quadrant operations. In fact, the operation in our series of cases would be better described as a ventral two-thirds coronal incision calculated to cut through those central and lower segments of white matter which McLardy and Meyer (1949) found to be the closest anatomical correlates of improvement after leucotomy.

GENERAL RESULTS.

The over-all results in this present series of 250 cases compare favourably with the findings in many other large group analyses, although it should be emphasized that two-thirds of our cases were suffering from affective disorders. All the patients have been under observation for at least one year after operation, those discharged being interviewed at home as well as the out-patient clinics.

A comparison of results between the lower and the full incisions, analysed in Table III, shows 70 per cent. lower quadrant cases discharged in the affective group of disorders as compared with 62 per cent. after full incisions. Such a discrepancy might well be accounted for by the tendency to favour a full incision for the relatively severe cases. Yet it would seem that the lower incision will produce

results equal to that of the full incision in selected cases. In the schizophrenic and psychopathic sub-groups there is little significant difference in the results of the two types of operation, and we therefore propose to pool the combined results and consider the group as a whole, comparing it with other large group results, and mentioning the type of incision only where it seemed to have significance.

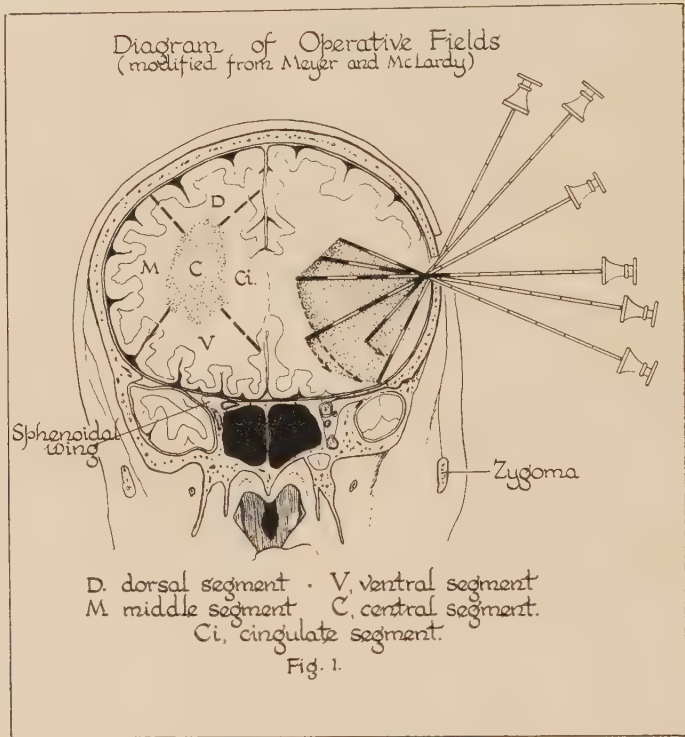


FIG. 1.—Diagram of operative fields (modified from Meyer and McLardy). D, dorsal segment. V, ventral segment. M, middle segment. C, central segment. Ci, cingulate segment.

TABLE III.—Comparative Results in Diagnostic Groupings of Full and Lower Incision.

	Total No. of cases.	Sex.		No. of operations.		No. of discharges.		No. of relapses.		Per cent. still discharged.	
		M.	F.	Full.	Lower.	Full.	Lower.	Full.	Lower.	Full.	Lower.
Affective	146	25	121	45	101	32	79	4	8	62	70
Schizophrenic	64	33	31	48	16	16	7	3	2	27	31
Paraphrenic	8	3	5	8	—	2	—	—	—	25	—
Psychopathic	26	11	15	17	9	3	2	—	1	17	11
Neurotic	6	2	4	3	3	3	3	—	—	100	100
Totals	250	74	176	121	129	56	91	7	11	40	62

In assessing the results of leucotomy Stengel (1950) utilized the useful concepts of “relative” and “absolute” as applied to degrees of recovery, and we have followed this method in drawing up Tables IV and V illustrating the results of operation in this series of cases. Relative results are related to the severity of the patient’s pre-operative condition, graded as symptom-free, much or slightly

improved. Such relative results are shown in Table IV, in which the cases are grouped according to diagnostic categories. The affective disorders constituted the largest group with 146 cases, and of these 30 per cent. were symptom-free and 42 per cent. were much improved. In the schizophrenic group of 64 cases, only 3 per cent. could be considered symptom-free and 17 per cent. much improved. Although only 2 per cent. of the affective disorders were not improved by operation, there were 40 per cent. of failures in the schizophrenic group, thus indicating the poor prognosis in this condition. The improvement-rate for the 250 cases was 81 per cent.

TABLE IV.—*Relative Results in 250 Leucotomies.*

Reaction types.	Total No. of cases.	Symptom-free.		Much improved.		Slight improvement.		Not improved.		Died (direct).	
		No.	%.	No.	%.	No.	%.	No.	%.	No.	%.
Affective .	146	42	30	61	42	34	23	4	2	5	3
Schizophrenic .	64	2	3	11	17	25	40	26	40	—	—
Paraphrenic .	8	—	—	1	15	3	35	4	50	—	—
Psychopathic .	26	—	—	7	27	12	46	5	19	2	8
Neurotic .	6	—	—	3	50	1	17	2	33	—	—
Totals	250	44	18	83	33	75	30	41	16	7	3

TABLE V.—*Absolute Results : Patients Discharged.*

Reaction types.	Total operations.	Total discharges.		Grade I discharges.		Grade II discharges.		Died after discharge. (No.)	Relapsed ; readmitted.		Still discharged.	
		No.	%.	No.	%.	No.	%.		No.	%.	No.	%.
Affective .	146	111	76	83	56	28	19	3	12	10	100	68
Schizophrenic	64	23	36	6	10	17	27	—	5	21	18	28
Paraphrenic .	8	2	25	1	12	1	12	—	—	—	2	25
Psychopathic .	26	5	19	2	7	3	11	—	1	20	4	15
Neurotic .	6	6	100	3	50	3	50	1	—	—	5	83
Totals	250	147	59	95	38	52	21	4	14	9	129	51

Figures in brackets represent relapses discharged again.

Absolute results, on the other hand, indicate the measure of the return of the patient's condition to what he was prior to the onset of illness, and to the standards of mental health as judged by the relatives on his return home. Such results are reflected in the discharge-rates as shown in Table V, the degree of recovery being indicated by Grades I and II. The former denotes a good remission of symptoms, a full adaptation to home environment with little or no disturbing personality defects. Under Grade II is placed those patients showing only a partial remission of symptoms, a moderate adaptation to home life, little or no occupation, and in some cases disturbing personality defects. The significant feature of Table V is the high Grade I discharge-rate of 56 per cent. in the affective disorders, and the disappointing results in schizophrenia with only 10 per cent. The Grade II patients are of variable stability, discharge depending more upon the tolerance and sympathy of the relatives, so that in this group there are always potential relapses and readmissions. Most of the discharged schizophrenics belong to this category. Analysis of results in the other groups is shown in the tables, but their numbers are too small for valid comparisons, and will be briefly considered under their respective headings. We are inclined to the view that absolute results are the only ones worth considering, and what matters most is whether the patient can be restored to a useful life outside the hospital.

RESULTS ACCORDING TO DIAGNOSTIC GROUPS.

Affective Disorders.

It is well recognized that the best results from leucotomy are found in the affective reaction types, particularly in the involutional melancholias and agitated depressions. Thus a review of the literature by Crown (1951) revealed good results

Aggressive Psychopaths.

In a group of 26 psychopaths of varied etiology but mostly epileptics, full leucotomy was carried out in 17 cases, and a lower incision in 9. The numbers are rather small for valid comparison, although the results favoured the full incisions. Improvement was obtained in 73 per cent., but only 5 patients could be discharged, and one of these relapsed. There was complete failure in 7 patients. McKay (1948) similarly reports improvement in two-thirds of his group of cases, with only an occasional discharge from hospital and full remission of aggressive trends.

Psychoneuroses.

Only six cases of this type were operated on, but three of these were much improved, including two obsessional and one anxiety case. The other three cases were hypochondriacs who showed little or no improvement.

FOLLOW-UP OF DISCHARGED PATIENTS.

Out of the 129 patients still at home in April, 1951, all but 8 had been discharged for at least twelve months, and 40 for two years or more. During interviews with these patients at the clinics and their homes we were enabled with the help of relatives to form a judgment of their readjustments to life both at home and at work. It was found that 96 patients or 70 per cent. of the total discharges were working at their former occupations, adjusting at Grade I level, and this proportion was approximately the same in both the lower and the full section types of operation. No one was doing work of high calibre before they broke down, and the majority found no difficulty in resuming their occupation, especially as this was often looking after the house and family. In Table X an analysis is made of the work carried out by the 96 fully occupied patients. It will be seen that 64 females are performing household duties satisfactorily and 32 patients are in paid jobs. Fig. 2 shows the percentage of discharged patients with good or poor work adjustments in the different diagnostic categories.

TABLE X.—*Working Status of Grade I Discharges.*

Full time occupations.	Male.	Female.	Total.
Household duties	—	64	64
Labouring	9	—	9
Factory	2	5	7
Typists	—	3	3
Tool making	2	—	2
Clerks	—	2	2
Domestics	—	2	2
Salesman	1	—	1
Boiler fireman	1	—	1
Bakery	—	1	1
Gardening	1	—	1
Rope splicing	1	—	1
Nursing	—	1	1
Army (R.A.S.C.)	1	—	1
Totals	18	78	96

Much has been written regarding personality changes following leucotomy, and it is uncertain how much is due to loss of control over pre-morbid traits, or to actual defects created by frontal lobe damage. We have found very few instances of disturbing personality defects in our patients discharged after lower quadrant incisions, and it is our impression that such disturbances are more likely to arise after full incisions, particularly if these are in a posterior plane. Partridge (1950), for example, found some frontal lobe defects in most of the discharged patients, as evidenced by a reduction of drive, activity and initiative, the patient being less critical of himself and others.

The difficulty of assessing the mental disabilities following leucotomy is well known, and there is often no decline of "test intelligence." Impairment of creative thinking or judgment in complex situations may have been present in our cases, but the level of adaptation required on discharge home was usually of such simple

character that difficulties seldom arose. This was certainly true of our elderly melancholic cases.

Out of the total of 147 discharges, 18 patients relapsed and were returned to hospital. Four of the relapsed melancholics soon returned home again after a short stay in hospital, and at the time of the final assessment 129 patients or 51 per cent. were still at home, 4 cases having died in the meantime. The relapse-rate was therefore 9 per cent., split up into 7 per cent. for the affective disorders

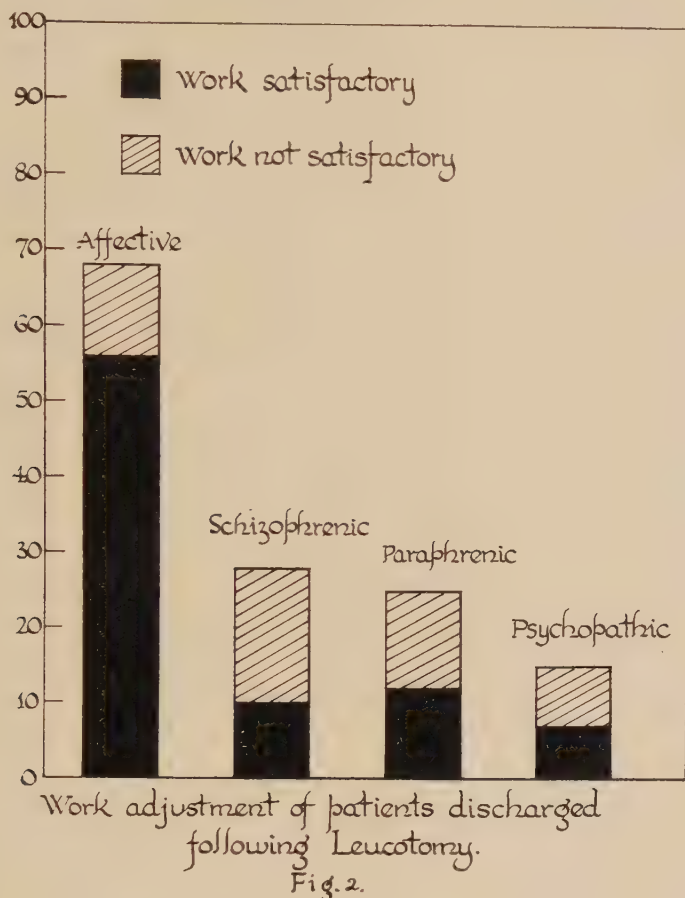


FIG. 2.—Work adjustment of patients discharged following leucotomy.

and 21 per cent. in the schizophrenics. Relapses were found to be particularly common (13 per cent.) in the recurrent melancholic group. One half of the 18 patients who relapsed after discharge did so in less than six months, but the others remained at home for longer periods, the maximum being $3\frac{1}{2}$ years.

POST-OPERATIVE COMPLICATIONS.

The total number of deaths in this series was 17, and of these, 7 could be considered as directly attributable to the operation, thus giving a direct mortality rate of 3 per cent., cerebral haemorrhage accounting for 4 of the 7 direct deaths.

Major fits occurred post-operatively in 14 cases or 6.6 per cent. of 210 non-epileptics. Although the numbers are small, analysis suggests that seizures are less frequent after lower incisions, the incidence being 5.1 per cent. against 8.6 per cent. after the full operations. No fits occurred in the small series of 16 schizophrenics submitted to a lower incision. In the affective disorders the incidence of

epilepsy was 5.0 per cent. after a lower incision, and 11.1 per cent. after full leucotomy. An analysis of the time of onset of the seizures further suggests that there is a greater tendency for the full leucotomy cases to develop "late seizures," i.e., longer than one month after operation, presumably as the result of scar-formation near the pre-motor area. Hofstatter *et al.* (1948) found no epilepsy in 85 patients after the low incision. Egan (1949) found two instances in 52 cases.

Urinary incontinence was rarely seen in our series of cases, and did not persist beyond the period of surgical convalescence except in a few deteriorated schizophrenics. A few elderly melancholic patients complained of urgency of micturition.

DISCUSSION.

The main purpose of this paper is to review the results obtained by a modified prefrontal leucotomy using a coronal incision limited to the central and lower segments of the frontal lobes. Our cases consisted of a mixed group of psychotics, mainly elderly melancholics, and an opportunity was taken to compare the results with those found in a standard full leucotomy. The main conclusion derived was that even allowing for a natural bias in selecting the milder cases for the limited incision, the results on the whole showed little difference between the two types of operation, but demonstrated most certainly that the lower quadrant incision is adequate in the affective disorders of later life.

The lower quadrant operations reported by other investigators seem to have been devised to sever the lower or orbital segments only, but it seems likely that fibres in the central segments are also cut and, indeed, we suggest that it is better to do so. The development of the lower quadrant leucotomy seems to have arisen from observations on frontal lobe injuries, which suggested that a special significance should be attached to the orbital regions in relation to emotional states, and in the early days of leucotomy Freeman first experimented with the "core method," and found that cores placed in the lower parts of the frontal lobes produced a higher incidence of good results than those placed in the upper region. It was considered that injury to the orbital region tended to produce a syndrome of euphoria, over-activity and extraversion—a triad of symptoms which might counter-balance those found in many types of psychosis.

Hofstatter *et al.* (1945 and 1948) reported excellent results in 22 patients of paranoid and schizophrenic type, and also in a later group of 85 patients. They used a low coronal incision from a point 5 cm. above the zygoma, and this probably does not involve fibres of the central segment. Dax and Radley-Smith (1946), using variously placed minimal incisions, found the highest percentage of good results in a low vertical incision. Reitman (1948) further analysed these cases, and found the results to be better than any section of other areas of the frontal lobe.

Egan (1949) studied a group of 52 cases, mostly schizophrenics, in which a low vertical incision was performed, combined with a mid-zone horizontal cut designed to isolate the orbital lobes. The measurements used for point of entry are not given, but the results were considered to be inferior to the standard coronal incision, particularly in paranoid schizophrenia. Freeman and Watts (1950) advocate a lower quadrant coronal incision in the mild psychoses.

There is considerable clinical evidence, therefore, in favour of the low vertical incision for use as a minimal leucotomy procedure, although its precise evaluation cannot be determined without correlation of clinical with anatomical findings. Much valuable work in this direction has been carried out by Meyer and McLardy (1949) on the brains of patients dying some time after leucotomy. These authors have, in addition to stressing the great variability of lesions produced by leucotomy, attempted to correlate the clinical improvement with the site and extent of the lesions found at autopsy. For the purpose of comparison they divided the coronal surface of the frontal lobes into five segments (Fig. 1), including a central and ventral or orbital segment. Their analyses failed to support the contention of specific psychological changes following orbital involvement, and they also indicated that no given coronal segment was always involved when improvement occurred. More segments were involved in the improved than in the unimproved group, but improvement correlated best with incision of the central and, to a lesser degree, the orbital segments.

The importance of the central segment is evident, since it collects fibres from most areas of the prefrontal cortex, and would therefore suggest itself as a con-

venient site for a minimal incision. On the other hand, the anatomical investigations suggest that the "optimum incision" should include the orbital as well as the central segment, and in our series of cases such an incision did in fact prove to be just as effective as the standard full operation. It is recognized that apathy constitutes one of the undesirable sequelae of the more posteriorly placed incisions, and in the full coronal incisions there may be a tendency to position the upper part of the cut too far back. This may be desirable in the aggressive and excitable patients, as is suggested by Dax and Radley-Smith (1946), but when apathy already predominates, it would seem that the full incision is better avoided.

Apart from the above-mentioned points, the results in our two groups of cases, one with a full and the other with a low coronal incision, were essentially the same, and compared favourably with the general average results from leucotomy reported by other investigators. Indeed, there has been a surprising constancy in the excellent post-operative results following the diverse procedures executed on the frontal lobes on patients with tension states. In this series there is a high percentage of affective disorders and a few schizophrenics. Most of these cases have undergone a smaller and more anteriorly placed incision than is customarily advocated, and our results would seem to demonstrate that in cases of depression, a lower two-thirds incision will, in the majority of cases, effect a satisfactory result without producing any personality defect. This was brought home to us by the attitude of relatives and people with whom the discharged patients live. When these people were questioned closely it was difficult to obtain any admission or indication that the patients fell short in adjusting themselves to their environment or life situation, in fact, in many cases the relatives insisted that the patient had now become much easier to live with than ever before. During the outside follow-up we could not help but be impressed by the gratitude of all concerned.

When this follow-up was started one of the authors had considered abandoning this closed procedure, but the universal good results of these discharged patients made it quite obvious that the operation was justifiable, for it should be borne in mind that many of these patients had already had two or three courses of shock therapy before leucotomy was considered. With this experience we have not hesitated to resort to leucotomy somewhat earlier, a procedure which can only be justified if one is certain to avoid any personality damage.

The percentage recovery and discharge figures worked out in these cases came somewhat as a surprise, and it would seem that good results can be effected in this type of material, provided that sufficient thalamo-cortical fibres are destroyed, without interfering with any particular aspect of the patient's personality. Such a destructive operation can only produce a favourable result in patients who have been well integrated and who have not broken down until comparatively late in life. The aged agitated melancholic will react better than any other after operation, provided his cerebral blood-vessels are not too arteriosclerotic. The reactive depression occurring as a sequel to life's stresses and strains does better than cyclothymic states, but a schizophrenic patient who has never reached an adult integration of the personality cannot be expected to gain much benefit by a destructive operation.

SUMMARY.

The use of minimal incisions in the technique of prefrontal leucotomy is discussed, with particular reference to the lower quadrant incision and its correlations with clinical and anatomical studies.

It is suggested that the lower quadrant coronal leucotomy is an effective minimal operation provided that the central as well as the orbital segments of white matter are cut, and that it is particularly suitable for states of chronic melancholia.

These conclusions have been drawn from a clinical assessment of 250 consecutive leucotomies performed by the same surgeon on a mixed group of psychotics suffering in two-thirds of the cases from states of melancholia. A comparison was made of the results from a complete as opposed to a lower two-thirds coronal incision, all cases being followed up for a period of one to eight years. At the time of final assessment 70 per cent. of 129 patients still at home had made good social recoveries.

There was little difference between the over-all results of the two types of operation, the combined group of 250 cases showing 81 per cent. improved, and a final discharge rate of 51 per cent., including 68 per cent. for affective disorders

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There was little difference between the over-all results of the two types of operation, the combined group of 250 cases showing 81 per cent. improved, and a final discharge rate of 51 per cent., including 68 per cent. for affective disorders

and 28 per cent. for schizophrenics. Excluded from these figures is 9 per cent. of discharges relapsed and readmitted to hospital. In the melancholic group the relapses were confined to cases with a history of recurrent attacks.

The operative mortality rate was 3 per cent., and there was a 6.6 per cent. incidence of post-operative epilepsy.

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CORTISONE IN THE TREATMENT OF SCHIZOPHRENIA.

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INTRODUCTION.

RECENT research has given rise to the hope that the secretory products of the adrenal cortex might be useful in the treatment of schizophrenia.

Two main lines of research have stimulated renewed interest in the role of the adrenal cortex in the pathophysiology of schizophrenia. A number of investigations have produced evidence that the responsivity of the adrenal cortex of schizophrenic patients to stress is lower than that of normal controls (Freeman *et al.*, 1944; Hoagland *et al.*, 1946; Pincus and Elmadjian, 1946; Pincus *et al.*, 1949).

Another series of investigations has shown that adrenocortical activity is stimulated by insulin coma therapy, electronarcosis and electroconvulsive therapy (Hemphill and Reiss, 1942; Mikkelsen and Hutchins, 1948; Rees (1949a); Parson *et al.*, 1949).

Cranswick and Hall (1950) reported that desoxycortone acetate and ascorbic acid appeared to be therapeutically valuable in schizophrenia. Rees and King (1951) carried out a controlled investigation on the treatment of schizophrenia with desoxycortone acetate and ascorbic acid, and found no evidence that the method was of any therapeutic value. It was pointed out that the investigation did not preclude the possibility that other products of the adrenal cortex might be therapeutically useful in schizophrenia.

The present paper describes a controlled investigation in the therapeutic value of cortisone administration in schizophrenia.

We are indebted to Dr. Ernest Evans, Consultant Physician, East Glamorgan Hospital, for making available a supply of cortisone for the investigation.

EXPERIMENTAL POPULATION.

The study was carried out on a group of 12 schizophrenic patients (6 male, 6 female), consisting of six pairs, matched for age, sex, clinical status, duration of illness and previous treatment.

METHODS.

1. *Clinical assessment.*—A detailed investigation of clinical status was carried out on the group. An item sheet of some 200 items relating to social, family and personal history, personality, aetiology and symptomatology was completed for each patient. Various clinical features and components of schizophrenic symptomatology were rated on a 7-point scale by the method of Rees (1949b). This detailed analysis of clinical status permitted an accurate matching of patients into pairs, one member of the pair for treatment and the other for control purposes.

2. *Assessment of recovery or improvement.*—In addition to the above detailed clinical assessment, a rating scale consisting of 14 traits relating to behaviour and symptomatology was completed before, during and after treatment. This method, consisting of making ratings of traits in terms of deviation from the normal, provides a quantitative expression of the patient's behaviour and clinical state. The sum total of the scores gives a convenient index of abnormality, permitting a quantitative expression of any change in symptomatology or behaviour during the period of observation. Doctors' and nurses' reports made independently of the above methods were also available.

3. *Psychological tests.*

(a) *Personal tempo.*

In view of clinical observations that changes in personal tempo appear to develop during cortisone therapy, the following tests were applied :

- (i) The number of triangles that could be drawn in 30 seconds.
- (ii) Enumeration of objects in 30 seconds, e.g., things to eat, birds; flowers.
- (iii) Number of responses to coloured Rorschach card in 30 seconds.
- (iv) Number of responses to uncoloured Rorschach card in 30 seconds.

(b) *Persistence.*

As a measure of persistence, the time the patient could hold outstretched leg with knee 3 in. above a chair was carried out according to the method of Eysenck (1947).

4. *Physiological tests.*—These included eosinophile counts, blood pressure and water intake and output records.

5. *Electroencephalography.*

The above tests were carried out before, during, and after the period of cortisone administration.

METHOD OF ADMINISTRATION AND CONTROL PROCEDURES.

The following procedure was employed : sterile water injections were given to both members of the paired patients for the first week, during which time all the tests were carried out. During the second week cortisone was given to one member of the pair and saline injections were continued with the other member.

Cortisone was given intramuscularly in divided doses amounting to 300 mgm. on 1st day, 200 mgm. on 2nd day, and 100 mgm. on the 3rd and 4th days.

RESULTS.

1. *Clinical status, symptomatology and behaviour.*—No significant improvement was found in any of the patients. One patient receiving cortisone became temporarily worse, returning to his previous state after termination of cortisone therapy.

2. *Psychological tests.*—No significant changes occurred in the tests of personal tempo or persistence.

3. *Physiological tests.*—In all patients receiving cortisone there was a marked fall of circulating eosinophiles, indicating that the cortisone had been absorbed and was active. No significant changes in blood-pressure or water balance occurred.

4. No change in electroencephalograph recordings was noted.

DISCUSSION.

Although there is considerable evidence that adrenocortical activity is stimulated by various physical methods of treatment, such as insulin coma therapy, electroconvulsive therapy and electronarcosis, it is not yet clear what role, if any, this plays in producing improvement or recovery. Hoagland *et al.* (1950) maintain that the adrenal cortex is stimulated by adrenocorticotrophic hormone (A.C.T.H.) released endogenously during shock methods of treatment. Hoagland *et al.* (1950) treated five schizophrenic patients for 3 weeks with daily doses of 100–200 mgm of A.C.T.H. without significant change apart from transient improvement in one patient who relapsed later. They concluded that it was not likely that A.C.T.H. would prove to have any therapeutic value in schizophrenia, and the beneficial effects of E.C.T. might involve entirely different processes.

The results of our clinical trials provide no evidence to suggest that an endogenous release of cortisone like substances from the adrenal cortex produced by insulin coma or electroconvulsive therapy is the underlying process responsible for improvement or recovery. Our findings are similar to those of Hoagland *et al.* (1950) with A.C.T.H., and give no confirmation of the recent report of Cohn and Karnosh (1951) that cortisone produces striking improvements in chronic schizophrenia.

The precise role of the adrenal cortex in the pathophysiology of schizophrenia has yet to be elucidated. There is an urgent need for further research in the effects of adrenocortical products on brain metabolism and their significance in various shock methods of treatment.

SUMMARY.

(1) The experimental population of the study consists of 12 schizophrenic patients (6 male, 6 female), comprising 6 pairs matched after detailed clinical analysis for age, sex, clinical status, duration of illness and previous treatment.

(2) All patients were given injections of sterile water for the first week during which all tests were carried out. During the second week cortisone was given intramuscularly in divided doses as follows: 300 mgm. on the 1st day, 200 mgm. on the 2nd day, and 100 mgm. on the 3rd and 4th days.

(3) Psychiatric rating scales, psychological tests of personal tempo and persistence, and physiological tests such as eosinophile counts, blood-pressure and water balance estimations and electroencephalography were carried out before, during, and after the period of clinical trial.

(4) No significant improvement was noted on the patients receiving cortisone therapy by clinical observation or by means of psychiatric rating scales. One patient became temporarily worse during cortisone therapy and returned to his previous state afterwards.

(5) No significant changes occurred in psychological tests for personal tempo and persistence or in blood-pressure or water-balance measurements.

(6) All patients receiving cortisone showed marked decrease in circulating eosinophiles, indicating that the cortisone had been absorbed and was active.

(7) No changes in electroencephalograph recordings were noted during cortisone administration.

(8) The investigation provided no evidence to suggest that cortisone given by the method described had any material beneficial therapeutic effects in schizophrenia.

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PSYCHIATRIC ASPECTS OF EPILEPSY IN CHILDREN.*

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THIS report of about 150 children is based on recent experience gained in the Maudsley Hospital Children's Department, in which epileptic children are investigated at special sessions. Most of the patients were examined in the usual way on their first visit to the Department. A full psychiatric history was taken from the mother or other relation. Intelligence tests, electroencephalogram (E.E.G.) and physical examinations were carried out. Later, as indicated, further special tests, such as air encephalograms, were done.

It is important to note the type of patients discussed in this report, in view of the notorious difficulty of obtaining reliable statistics in such a subject as epilepsy, whose manifestations are so varied that any one hospital or clinic cannot expect to see a truly unbiased sample. Children referred to the Maudsley Hospital nearly always show some behaviour disorder, but lack gross neurological signs and symptoms. Even in the case of epileptics a behaviour problem is frequently the presenting complaint, the actual seizures being a secondary problem. As the facilities for investigation are better than in many other clinics, cases are frequently referred from other hospitals for special investigation. This material, therefore, is undoubtedly heavily weighted by epileptics with behaviour problems. There are, on the one hand, disproportionately too few mentally normal children with epilepsy, and on the other, too few with epilepsy in association with grosser neurological disorders. No attempt is made, therefore, to give any statistics on the incidence of a particular symptom or sign within this group, as it is meaningless in relation to the whole body of epilepsy in children. The recent outstanding book by Bridge (1950) gives a very fair picture of epilepsy in childhood.

The aetiological factors may be divided into two groups: those within the social situation and those within the child.

FACTORS WITHIN THE SOCIAL SITUATION.

A child with epilepsy is not thereby absolved from the need for normal emotional development. He is, therefore, liable to all the difficulties inherent in this, which form the majority of problems seen at an ordinary child guidance clinic. All the usual factors which may produce disturbances in children, such as rejecting or over-protective parents, sibling rivalry, can be seen in the epileptic child. He, however, has his own special disability, which is an important source of disturbances in inter-personal relationships. The epileptic fit itself arouses great anxiety in the parents, and, apart from any other problems which the child might have, the fits themselves frequently produce parental over-protection or rejection. As usual, the parental attitude then reacts on the child, and a severe behaviour problem can arise, solely on the basis of these emotional disturbances.

FACTORS WITHIN THE CHILD.

Bridge notes that personality disorders are correlated only with environmental difficulties and not with factors within the child, when epileptic children are considered as one group.

The factors within the child are many and complex. Of first importance is the character of the epileptic "process," to use an intentionally vague term. It must be stressed that an epileptic seizure is a symptom, not a disease, and the

* Based on an address given to the Child Psychiatry Section of the Royal Medico-Psychological Association, February, 1951.

result of many physiological abnormalities, whose diversity is in part clearly seen in the E.E.G. Leaving aside the detailed physiology of epilepsy, it is sufficient to stress that many different types of seizures and E.E.G. patterns are found in epileptic children. Although there is no rigid correspondence between inter-seizure E.E.G. and fit patterns, there appear to be certain fairly distinct types of epilepsy, differing in aetiology, prognosis, treatment and clinical picture. These will be noted below.

The presence or absence of acquired brain damage is the second important factor. This term is used in the widest sense, covering not only physical trauma from birth onwards, but also the residual effects of infections, vascular accidents, gross congenital defects and other causes of microscopic or macroscopic brain abnormalities. As is well known, brain injury, especially if severe, may be followed by many symptoms, of which epilepsy is only one. These may be negative ones, in Hughlings Jackson's sense, for example, aphasia, hemiplegia, hemianopia; or they may be positive symptoms, perhaps better described as release phenomena, for example, hyperkinesis, irritability. Bender (1945) has clearly described the clinical picture sometimes seen, to which epileptic seizures may be added. About 20 per cent. of children in this series have definite brain damage, a rather lower figure than that found by Bridge.

The intellectual capacities deserve mention, although they are in fact partly dependent on the two first-mentioned factors of brain injury and the epileptic process. The intellectual level is usually of greatest clinical importance when the level of educability is below that of the ordinary school and above that of the defective colony, i.e., an I.Q. between 80 and 60 approximately. Problems also arise when there is a wide scatter of abilities in the intellectual sphere. Difficulties in reading and/or arithmetic are quite common in epileptic children, though whether more so than in the general run of psychiatrically disturbed children cannot be stated. A survey of speech difficulties in epileptic children showed them to be twice as common (nearly a quarter of the total) than in a control group of 200 non-epileptic, non-organic behaviour problem children (mental defectives were excluded from both groups). This may be compared with the well-known speech difficulties of adult chronic epileptics.

The body-build of children has more often been commented on than measured, but its importance cannot be ignored. The slightly built, retiring boy with *petit mal* seizures contrasts with the stockier build of the child with major seizures and an aggressive behaviour problem. The former also are prone to vasomotor instability, as shown by dermatographia, and sudden changes of skin colour and temperature.

CLINICAL VARIETIES OF EPILEPSY IN CHILDHOOD.

Several more or less distinct groups of epileptic children can be delineated, of which the most clear cut is the *petit mal* child already referred to. Such children are either small, blue-eyed, fair-haired boys, or rather darker, more untidy-looking girls whose epileptic seizures are almost exclusively of the classical *petit mal* variety, although some of them have occasional *grand mal* convulsions with childhood fevers. Their E.E.Gs. all contain three cycles per second spike and wave bursts, but are otherwise relatively normal. There is rarely any evidence of brain injury. In personality they are usually stubborn, but not overtly aggressive, and on the whole they are rather passive, serious minded, nice-mannered children. Their behaviour disorder is not of an aggressive or hyperkinetic character but shows itself mainly in what appear to be neurotic symptoms—nightmares, night sweats and anxiety attacks. They are inclined to be babyish and over-dependent. Their social situations also are curiously similar. This is the subject of further investigation at the present time with the psychiatric social worker, who has been particularly associated with the epileptic children's clinic. She has observed that mothers of these children are notable for their apparent verbal reasonableness, overlying a great deal of constant anxiety and over-protection. They nag rather than lose their temper. On the whole the family makes a good impression to the outside world, appearing steady-going, reasonably ambitious and fairly gentle.

Children with brain injury are in contrast to the *petit mal* child in almost every way. The brain injury in the majority of these children does not produce any gross neurological signs or defects, and their behaviour disorder cannot be attributed simply to frustration from such a defect. The syndrome can be seen most charac-

teristically after head injury, and has been well described by many others, particularly Bender (1945). They are usually violently aggressive, explosive, irritable children, unpredictable and variable from moment to moment. They may sanctimoniously complain about their difficulties, but continue to lose their tempers. Their span of attention and concentration is poor, although their I.Q. on testing is not usually much below normal. (Mental defectives secondary to brain injury will be discussed below.) They suffer from *grand mal* seizures and/or psychomotor attacks, but never classical *petit mal*. Their E.E.Gs. are either normal, or show specific, usually focal abnormalities. The severest behaviour disorders are associated with focal E.E.G. abnormalities in the temporal rather than the frontal regions. These patients often have a bad family history of psychopathy and their social backgrounds are unsatisfactory. These predisposing factors present before injury would appear to be almost as important as the actual injury in producing behaviour disorders. There have been, for instance, several brain-injured children in this series with normal personalities, and in all these cases there was a stable family and social background. Such cases show the bias of the Maudsley material, since patients without a behaviour problem would tend to be referred to neurological hospitals. Of all the behaviour problem children who come for treatment these brain-injured children present by far the greatest problem, not so much in the control of the fits, but in the relief of the behaviour disorder, particularly in regard to school placement. An epileptic colony will not admit them because of their behaviour disorder, and the maladjusted school will not take them because of the epilepsy. They very frequently cannot remain at home, but they are not certifiable under the Mental Deficiency Acts. Excluded from one school after another, their educational level falls lower and lower, and their rejection from one environment after another still further increases their behaviour problem. There is at the present time urgent need for some special place to which these children can be admitted, not only for their own sakes, but to enable important research into the problems which they present to be undertaken.

Mentally defective children fall into two main groups. There are those in whom the defect is secondary to severe brain injury, which also causes epilepsy of *grand mal* type, often with myoclonic jerks and peculiar partial seizures. Such children sometimes show a hyperkinetic behaviour disorder, but their social disposal is usually to a mental defective colony. There are also a few defective patients, in which the mental defect appears to be unrelated to brain injury, and may possibly be secondary to the epileptic process, which in these children appears to undergo a somewhat malignant course. They are subject to *grand mal* seizures, psychomotor attacks and periods of disturbed behaviour, which are probably post-epileptic confusional states. Some of them suffer from *status epilepticus* with great frequency, and, although their fits are fairly easy to control, their mental state is little improved. Their E.E.Gs. show a large amount of irregular epileptic activity in all areas of the brain. The social situation is often over-protective rather than rejecting, and there are occasional rather pathetic families whose mothers have sacrificed the interests of their other more normal children to the demands of the defective epileptic one. The psychiatric problem in these cases is not in the child, but in the parents, who have to be persuaded towards a more realistic and balanced outlook on the whole family situation.

Not more than half the children can be classified into the above groups, the rest being more heterogeneous. It is not necessary to dignify the groups with particular names or characterize them as separate diseases: they represent rather particular combinations of brain injury, I.Q. level, fit tendency and social situation which appear to occur together sufficiently frequently to produce similar patients.

PSYCHIATRIC ASPECTS OF THE SEIZURES.

The biochemical and physiological changes associated with fits are not relevant to this discussion. The relationship of the time of occurrence and character of epileptic seizure to the psychological state of the patient is sometimes of interest. The character of the attack sometimes may be related to some psycho-pathological event, but less often than in adults. This is particularly true if the disturbance of consciousness in the fit is incomplete, as is usual in seizures originating in the temporal lobe. In the dreamy, confused state which may be associated with a seizure, aggressive and sexual feelings may reach overt expression or appear as vivid, terrifying phantasies. This is probably the reason why psychomotor

attacks may be more often connected with psychological disturbances than are pure *petit mal* or *grand mal*. In these latter types of attack the onset of the disturbance of consciousness is complete and instantaneous, and the return of consciousness is either equally instantaneous, as in the case of *petit mal*, or usually succeeded by a period of sleep as in *grand mal*. It is of interest that there appears to be no connection between epilepsy and schizophrenic symptom pictures such as is quite common in adults. This is probably owing to the relative rarity in children of temporal lobe epileptic foci, and psychomotor types of seizures, which are the commonest epileptic manifestations seen in adults in association with paranoid ideas, hallucinations and schizoid personality traits.

Frank psychotic episodes seem to be rare in epileptic children and only six have so far been seen. (Bridge reports an even lower incidence—only two in over seven hundred cases). Periods of confusion with hallucination and thought disorders are occasionally seen following fits, especially before they are controlled by drugs. In one child of rather low intelligence a psychotic episode with delusions and obscene behaviour, quite out of keeping with his previous personality and home background, was precipitated by phenobarbitone.

Petit mal seizures (as distinct from temporal lobe attacks) in which there is a sudden absolute loss of consciousness have a different relationship to psychological events. As has also been observed by others (e.g., Wayne Barker *et al.*, 1950a and b), they may act as an escape mechanism from an emotionally disturbing situation. One parent, for example, said that her child with infrequent *petit mal* seizures would have an attack if he were asked a question too difficult for him to answer.

Mittelman (1948) has conveniently summarized many views on the psychopathological significance of seizures to the patient. He himself emphasizes that the experience of recurrent loss of control adds a special colouring to submissive and masochistic strivings. Such personality traits would seem more common in children with *petit mal* than with *grand mal* and psychomotor seizures, and yet it is probable that the latter are much more aware of the onset of their seizures than the former; thus, it is not certain that the actual experience of a seizure operates in this way.

SOCIAL AND PSYCHIATRIC ASPECTS OF TREATMENT.

The interaction of the social background and the epileptic fit, to which reference has already been made, was well discussed by Tylor Fox (1951). It is important to realize that the child's own attitude to his seizures is very largely influenced by the parental attitude, that is to say, they tend to be anxiety-producing if the parental attitude is anxious. Younger children especially are often matter-of-fact about their attacks. Adolescents tend to blame fear of seizures as a cause of emotional disturbances, but the position is usually more complex.

The parental handling of an epileptic child is so important that it is almost true to say, paradoxically, that the commonest reasons for recommending a child to be sent to an epileptic colony are disturbances at home (or secondarily at school), and not the actual seizures. The majority of teachers are also willing to have epileptics, particularly if the case is explained to them, and it is usually a behaviour disorder and not the seizures which is the reason for school recommending a colony.

A ward which specializes in investigating the problems of epileptics has been found most useful for these children (reported to the International League against Epilepsy, Jan. 1951). In this way the relative importance of social and intrinsic factors in the production of a behaviour disorder can more quickly be assessed. The observation by the parents of how their child can behave in tolerant surroundings is often a help to them.

The problem of medical treatment is one which cannot be covered completely here. The pros and cons of the different drugs at present available would in themselves occupy a whole paper. It appears, however, that phenobarbitone is often contraindicated. Psychotic episodes have been precipitated by its use, and increased irritability is very common. Phenytoin is undoubtedly the first drug of choice for the control of *grand mal* seizures. The effect of amphetamine in these children is often dramatic and paradoxically opposite to that in adults in that it definitely tends to quieten rather than excite children. Its most important indication is hyperkinesis and irritability (see Bradley, 1950). The effect of

amphetamine on behaviour problem children generally is at the moment under special study at the Maudsley Hospital.

Individual psychotherapy appears only occasionally indicated. In the present state of knowledge it is definitely not a practicable treatment for actual epileptic seizures *per se*. The indication for its need is the presence of a behaviour disorder or neurotic symptoms, though treating these may well result in a correlative diminution in the frequency of attacks. However, the psychiatric social worker has a very important part to play. The parents nearly always have a large number of specific fears and anxieties about epilepsy, which have to be discussed over and over again. Fears of the child becoming a criminal or insane, or injuring or killing himself in a fit, are present in most mothers. There are anxieties about its transmission to other children, and sometimes a large amount of self-reproach on the part of the parent, particularly if the fit appears to follow some accident, or even emotional incident. An allaying of these anxieties with a general reduction in family tensions quite often reduces the number of seizures—especially in children with *petit mal*.

DIFFERENTIAL DIAGNOSIS OF ATYPICAL SEIZURES.

The last problem to be discussed is that of the differential diagnosis of epileptic seizures. The varieties of attack and behaviour seen can be conveniently divided into two groups. Firstly, there are attacks with an apparent disturbance of consciousness which are possibly epileptic or post-epileptic, the hysterical attack, the faint and fugue being the most usual examples. (Patients with attacks from disease or functional anomalies of the labyrinthine or cardiovascular systems tend to be referred to general or neurological hospitals.) Some of these are often very difficult to diagnose. The finding of possibly relevant psychopathology is clearly of no diagnostic importance in view of what has already been said. The E.E.G. in these cases may be mildly abnormal and therefore of no help. The recent advances in the "provocative techniques" (photic stimulation, metrazol, etc.) have been used at the Maudsley only on adults and adolescents. Within these age-groups the significance of positive results is by no means clear-cut. In children the interpretation is likely to prove even more difficult, as the tendency to fits is well known clinically to be much increased at younger ages (Nekhorocheff, 1950). In the clinical history the most reliable symptom of epilepsy is a primary disturbance of consciousness which is clearly apparent as a gap in the patient's memory, or of a definite account by observers of a period of blankness, confusion or uncoordinated actions, lasting a few minutes. Disturbances of consciousness can occur secondarily to a faint, so the exact conditions of any one attack must always be most carefully investigated. True epileptic seizures may occasionally be precipitated by such an anoxic mechanism in susceptible subjects.

The second group of symptoms referred to as being possibly epileptic are more in the nature of behaviour disorders—temper tantrums, enuresis and nightmares. Enuresis and nightmares are not more common in the present group of epileptic children than in the control group of non-epileptics already referred to, and they are almost always accompanied by other more obvious epileptic phenomena. There is a tendency to ascribe many such psychiatric symptoms to epilepsy, and the epileptoid character of irritability, poverty of initiative, etc., has a long history (see, e.g., Naville and Brantmay, 1935). There is, however, no evidence that a temper tantrum can occur during a partial or "diluted" epileptic process in the physiological sense. No such thing exists. The apparent diminution in full consciousness during, and the partial amnesia professed after very violent tantrums, have not the same physiological basis as in the epileptic fit. The possible animal analogue, the "rage reaction," seen for example from stimulation of the hypothalamus, is not an epileptic phenomenon. It is necessary in order to clarify these matters to resort again to Hughlings Jackson's principles of the levels of activities. The only epileptic seizures unaccompanied by disturbances of consciousness are the low level ones of *epilepsia partialis continua* and focal motor or sensory seizures. As soon as the seizures reach higher levels, consciousness and sensori-motor co-ordination are in some way disturbed, making directed activity extending over a period of time impossible. From the study of adult epileptics, Hill and Pond (1952) are convinced that co-ordinated, purposeful action cannot occur in a psychomotor seizure, though this may happen in a post-ictal confusional state.

Hill considers that behaviour such as temper tantrums can be regarded as "epileptic equivalents" only in the sense that a fit and a tantrum are seen as *alternative* mechanisms of discharge. The problem of what is discharged is made difficult by the lack of correspondence between physiological and psychological terms. It is not known what, physiologically speaking, is the emotional discharge in a tantrum, nor can the affective state of an epileptic in a fit be known. This does not imply that the emotional states "cause" epilepsy. It is rather that from some aspects epilepsy can be looked upon as a psychosomatic disease. The somatic predispositions can be utilized for psychological purposes, sometimes with good effect, as can be seen, for example, in attacks of epilepsy ending psychotic episodes. Likewise the behaviour of some epileptics is definitely worse when they have fewer fits. In spite of all laboratory advances, epilepsy still remains a clinical diagnosis, or perhaps it would be truer to say that epileptic attacks are those *spontaneous* seizures which by experience have been associated with epileptic discharges in the electroencephalogram: and an epileptic patient may show many other phenomena which may not be associated with epileptic discharges in the brain.

THE "EPILEPTIC CONSTITUTION."

It should be stressed again that the social situation is as important in epileptics as non-epileptics in the production of behaviour disorders. However, a study of epilepsy in children leads inevitably to the view that there are important constitutional differences between children which interact with the social situation to produce symptoms. The *grand mal* seizure and temper tantrums appear related, and may perhaps be seen as an expression of one common tendency of an overtly violent aggressive character. The incidence of temper tantrums was considerably higher in a group of such epileptics than in the control group of two hundred non-epileptics mentioned above. The *petit mal* seizure and neurotic symptoms may be another case of two facets of a fundamentally common mechanism. Thus, in addition to fit and behaviour being associated as alternative mechanisms of discharge, there is the possibility of another still deeper connection in that some abnormal brain activity may underlie both the fit tendency and the character of the behaviour disturbance. There are thus not one but probably several personality types found in association with epileptic fits.

In an article published after this paper was first read Bradley, (1951), attempts to divide the behaviour disorders of epileptic children into "primary expressions of disordered cerebral function" and personality reactions secondary to the illness and the attitude of those in contact with the child. The traits he describes as primary—erratic mood variability, hypermotility, irritability, short attention span and a relative mathematical disability—are not, however, seen in all epileptic children. Furthermore, he himself points out that they are often seen in children with organic brain damage without epilepsy. Such attempts at dividing symptoms into primary constitutional, and secondary environmental are unfortunately only too common in child psychiatry. No behaviour trait or disorder is ever either one or the other, but the product of the interaction of many constitutional and environmental factors such as is outlined here.

The concept of the epileptic constitution is by no means confined to human beings. Some early Italian workers (for instance, Amantea, 1921), showed that relative susceptibility to epilepsy varies much between dog and dog, and dogs easily provoked to an epileptic fit were on the whole more difficult, violent and harder to manage than the relatively non-epileptic dog. By combined psychological and physiological studies of patients it may, therefore, be possible to define more closely this problem of epileptic constitutions.

SUMMARY.

Children with epileptic seizures seen at the Maudsley Hospital Children's Department form the basis of this report. The psychiatric symptoms are considered in relation to factors within the child (brain damage, type of epileptic process, intellectual factors, body-build, etc.) and environment factors. Several clinical groups of patients are described, children with *petit mal*, with brain damage and with mental defect being the most important. The psychiatric aspects of seizure, of treatment and the problems of differential diagnosis are discussed. It is con-

cluded that there are several personality types commonly seen in association with epileptic fits which are the product of many constitutional and environmental factors.

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STUDIES ON THE PHYSIOLOGY OF AWARENESS: AN OXIMETRIC INVESTIGATION OF THE ANOXAEMIA ACCOMPANYING INSULIN COMA THERAPY.

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THIS investigation deals with the measurement, by a peripheral method of discontinuous spectroscopic oximetry, of the arterial blood oxygen saturation levels in a group of schizophrenic patients undergoing insulin coma therapy.

The association between tissue anoxia and insulin hypoglycaemia was first established by Campbell and Dudley in 1924. Dameshek and Meyerson (1935), using the arterio-venous oxygen difference method with the internal jugular vein as the source of venous blood, showed that the injection of insulin in coma doses was accompanied by an anoxaemia in the schizophrenic patients they studied. This work was confirmed by Himwich, Bowman *et al.* (1939), and in another paper Himwich (1951, p. 277) and his co-workers found that the correlation of progressively developing clinical symptoms with the decrease of cerebral oxygen uptake was a closer one than the correlation with the more acute fall in the blood-sugar curve. An important symptomatic aspect of insulin hypoglycaemia includes the progressive changes in the levels of consciousness accompanying the approach towards coma. Wilder (1943) has outlined some of these changes, and Frostig (1940) and Himwich (1951, pp. 258-265) have delineated these awareness thresholds and discussed their relationship to the Hughlings Jackson theory of the phyletic organization of the central nervous system. Thus, during the *first hour* following insulin injection, somnolence and lassitude appear to be associated with suppression of cortical and cerebellar activity; in the *second hour* further clouding of consciousness, sometimes with excitement, perceptual disturbances, periods of confusion, exacerbations of previously existing hallucinations and latent psychotic syndromes are seen; in the *third hour* motor restlessness and loss of consciousness suggest the release of basal ganglia and hypothalamus; in the *fourth hour* deepening stupor and depression of exteroceptive sensitivity indicate a probable release of the midbrain and suppression of pyramidal function; in the *fifth hour* the deep pre-mortal coma presages medullary release. Similarly, it is with awareness changes that many workers prefer to diagnose the "real coma" level in a patient under treatment. Thus Sakel (1937) held that coma was to be diagnosed when no further personal contact with the patient was possible, and Kalinowsky and Hoch (1946) agree that the real coma level is reached when it is completely impossible to awaken the patient.

The correlation between changes in the levels of awareness and those of the arterial oxygen saturation of the blood have been the subject of many investigations. This literature, especially from the psychiatric viewpoint, has been reviewed elsewhere (Lovett Doust, 1952). It has also been shown by the present writers (Lovett Doust and Schneider, 1952) that when the progress of natural sleep is followed, by a method of continuous photoelectric oximetry, through its various phases of gradually lessening degrees of consciousness, so successively greater depression in blood-oxygen saturation level occurs. The relationship between the effects of

experimentally imposed anoxic anoxia and the concomitant production of psychiatric symptomatology has also been demonstrated (Lovett Doust, 1951a). Here it was suggested that the changes in mental state could be predicted from a knowledge of oximetrically determined blood-oxygen levels, and conversely that these levels could be anticipated when patients showing similar "idiopathic" psychiatric changes in their mental state were examined by oximetric methods.

In the past every effort has been made to examine blood samples for their oxygen content taken from regions as close to the brain as possible. The previous work of the present writers referred to above has been largely concerned with the demonstration that changes in oximetric values obtained peripherally, by recording from the blood in vascular complexes of minute vessels situated in either the finger-nail fold or the pinna of the ear, bear an intimate relationship with those predicated for the cerebral circulation. The usefulness of oximetric methods lies as much in the fact that they are rapid and readily reproducible as in their non-traumatic nature to the patient. It is with the application of these methods to the twin problems of the association of anoxaemia both to the diminishing awareness present in insulin shock and to the essential identity of peripheral capillary oximetric findings and those of cerebral metabolism that this paper is concerned.

EXPERIMENTAL METHOD.

The technique for determining the arterial blood oxygen saturation levels was a peripheral one. It consisted of a method of discontinuous spectroscopic oximetry, the principle of which was discovered by Karl Vierordt in 1878 and developed by Ray (1946). Further refinements in the technique have been made (Lovett Doust, 1951a), and the method is now one of considerable accuracy and reliability (Lovett Doust, 1952). Essentially the procedure depends upon the fact that when the histaminized illuminated finger-nail fold is viewed through a pocket spectroscope and the α and β absorption bands of oxyhaemoglobin visualized in the spectrum, these bands disappear following occlusion of the peripheral circulation in a time interval highly correlated with the arterial blood oxygen saturation levels. Although the end-point of each determination is a subjective one, experience leads to a high degree of reliability, e.g., a very high correlation coefficient ($r = +0.92$) was obtained in a series of 285 simultaneous observations on a number of subjects using this method of spectroscopic oximetry, and comparing the results with those of a photoelectric oximetric instrument (Lovett Doust, 1951b).

Each assessment of an individual patient occupied a period of some 10 hours. The subject lay in bed in a side room off the main insulin ward of the hospital. The investigator arrived at 7 a.m. and proceeded to make spectroscopic oximetric observations at 5-minute intervals from that time. These consisted in the patient resting his arm, around which a sphygmomanometer cuff attached to a pressure bottle had been previously wrapped, on a conveniently placed bedside table. The nail-fold skin of the ring finger of the right hand was initially prepared by inuncting 2 per cent. histamine ointment (British Drug Houses, Ltd.) into it to ensure maximal vasodilatation of the part, and it was illuminated and heated by the presence of a 100 watt incandescent lamp held at about six inches from it in an adjustable holder. A single determination consisted in filling the sphygmomanometer cuff to a pressure well above that of the arterial blood-pressure from the pressure bottle reservoir in rather less than one second and at the same time starting a stop-watch. The end-point was taken to be equivalent to the visual disappearance of the absorption bands and the appearance of a homogeneous spectrum. The reliability of each individual measurement was frequently checked by repeating it within the five-minute period. Some difficulty was often encountered during the periods of sopor and coma owing to the restlessness of the subject, but it was found to be perfectly possible to keep the arm still for the very short time needed to take a reading.

Immediately following the oximetric observations in any one five-minute period, the respiratory rate per minute was determined. Although it was not practicable to measure the depth of the respiratory excursion, these estimates of rate provided an interesting correlate of the various phases of blood-oxygen variation.

Insulin, in a previously determined effective dose, was injected some 45 minutes following commencement of the day's experiment, and hence after the post-sleep resting levels had reached a steady state (Lovett Doust and Schneider, 1952).

Regular observations were continued throughout the phases of pre-sopor, sopor and coma until the attending clinician interrupted this by the administration of glucose. The latter was for the most part exhibited as an intravenous interruption, but in two cases it was given via a nasal tube, intragastrically. During this critical period of coma reversal and dramatic changes in consciousness, the oximetric determinations were made as frequently as possible, often at minute intervals. The post-glucose readings were continued until they stabilized, and were then discontinued to allow the patient to be fed and bathed: they were recommenced towards the late afternoon. It is important to emphasize that the clinical diagnosis, both of the changing psychiatric state of the patient and of the appearance and duration of sopor and coma, was made completely independently of the present writers by attending competent and experienced psychiatrists. The accuracy of these clinical judgments, in so far as the march of events following the injection of insulin was concerned, may be judged from their oximetric correlates in the results. No complications, such as spontaneous convulsions or "irreversible" coma, occurred during this investigation, but one patient, early in her course of treatment, did not go into coma on the dose of insulin given.

CLINICAL MATERIAL.

A total of 13 patients was investigated. All had been diagnosed as suffering from one variety or another of schizophrenia, after careful assessment over a period of weeks at the Maudsley Hospital. They were selected for the present study following their transfer to Bethlem Royal Hospital, and after deep insulin treatment had been proceeding sufficiently long for predictable comas to occur.

Of these 13 subjects, 6 were males and 7 females. Ages ranged from 18 to 47, with a mean of 28.0 years. Subdivision of the major diagnosis of schizophrenia common to all yielded 9 examples of schizophrenia, paranoid type, and 4 of schizophrenia, constitutional type; of these latter, 3 were classified as suffering from hebephrenia and 1 from dementia praecox simplex. Soluble insulin was administered in doses ranging from 90 to 400 international units and injected intramuscularly into the buttock. These doses had resulted in ranges of 3-30 sopors and 1-24 comas on previous occasions, and it can hence be seen that the patients included in this study numbered among them those in both early and late stages of their treatment. The individual details for each patient may be seen in Table I, which lists the basic data for each protocol.

RESULTS.

These may be seen in detail in Table I, and individual cases are exemplified in Figs. 1-4. Fig. 5 is a composite chart, in which the overall oximetric measurements are expressed as their range deviations against time. It can be seen that a progressive decline in peripheral arterial blood-oxygen saturation levels takes place following the injection of the insulin. This gradual depression of oximetric values occurs in a step-wise fashion, the initial mean resting level of 93.3 per cent. oxygen falling gradually, with fluctuations of about 1 per cent. during the course of some two and a half hours, to reach a pre-sopor level of 89.4 per cent. Here, in many cases, a further fall of 1.5 to 2.0 per cent. oxygen occurs, and it was at this point that the clinical psychiatrist detected the onset of the sopor state. This state of sopor persists for a varying period (mean = 58 minutes), the oxygen levels falling from 89.4 to 87.3 per cent. At this time a second decline ensues to levels around 86.4 per cent. oxygen and corresponding to the clinical assessment of the state of coma. The duration of coma was a matter for clinical judgment, but represented in most of the cases studied a period of 30 minutes. It was observed in some cases (e.g., Fig. 1, patient J. C—) that, in any event oximetrically, coma was a progressive state, since the levels underwent a further decline during this period. Coma was interrupted in 11 of the 13 patients by the intravenous infusion of 33.3 per cent. glucose solution. Usually 150 c.c. sufficed to bring the patient round, after which he was given 250 c.c. of orange-juice sweetened with glucose. The more frequent oximetric observations begun with the interruption of coma revealed (Figs. 1 and 2) a striking and rapid increase of oxygen levels. The mean maximal elevation was to 99.0 per cent. oxygen, but frequently levels of 100.0 per cent. were attained (Table I). This abnormally high value falls quickly in some 10 to 15 minutes to a saturation often equivalent to the pre-insulin resting

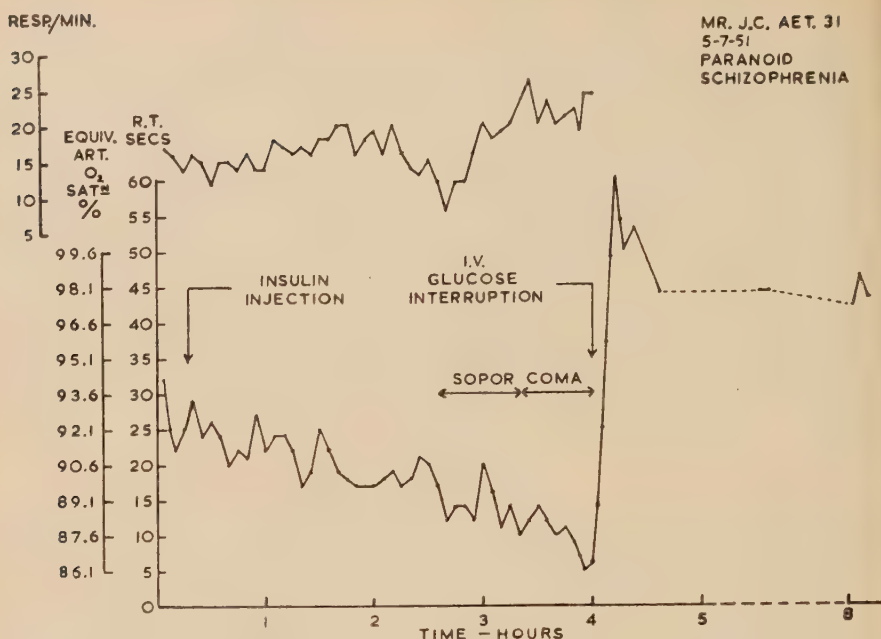


FIG. 1.—Typical results of oximetric monitoring of a case of paranoid schizophrenia through a morning's treatment with insulin coma therapy. Note the mirror image appearance of the respiratory rates as compared with the oxygen saturation levels. The "rebound phenomenon" is well shown, the oximetric rise following coma interruption being sustained at a value well above the pre-insulin resting level once the steady state has been attained. In this patient the raised final oximetric values coincided with improvement in the clinical condition.

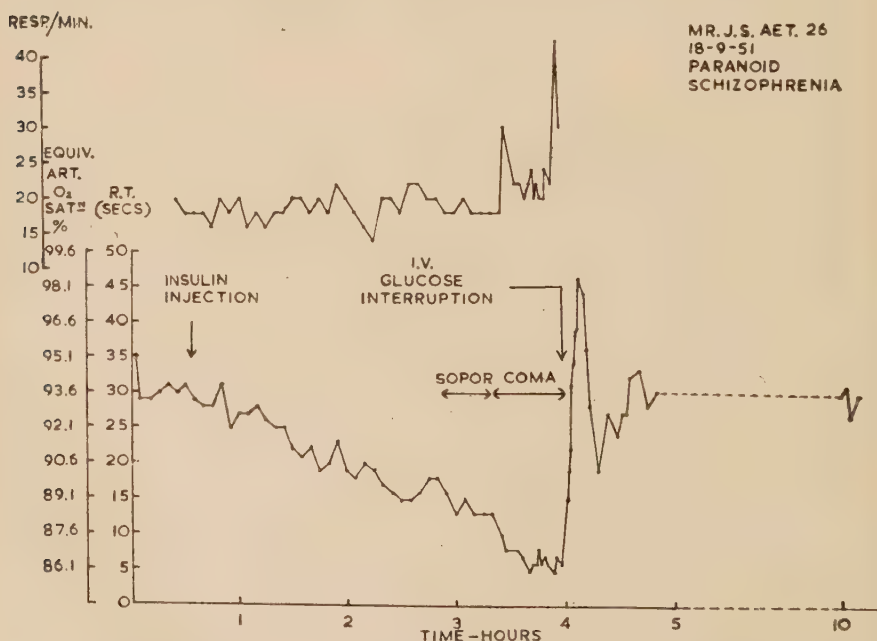


FIG. 2.—In this example the oximetric stages of sopor and coma are particularly well shown. The "rebound phenomenon" is less marked than in Fig. 1, and the final steady state values, equivalent to those of the pre-insulin resting period, corresponded with no essential clinical change in the patient.

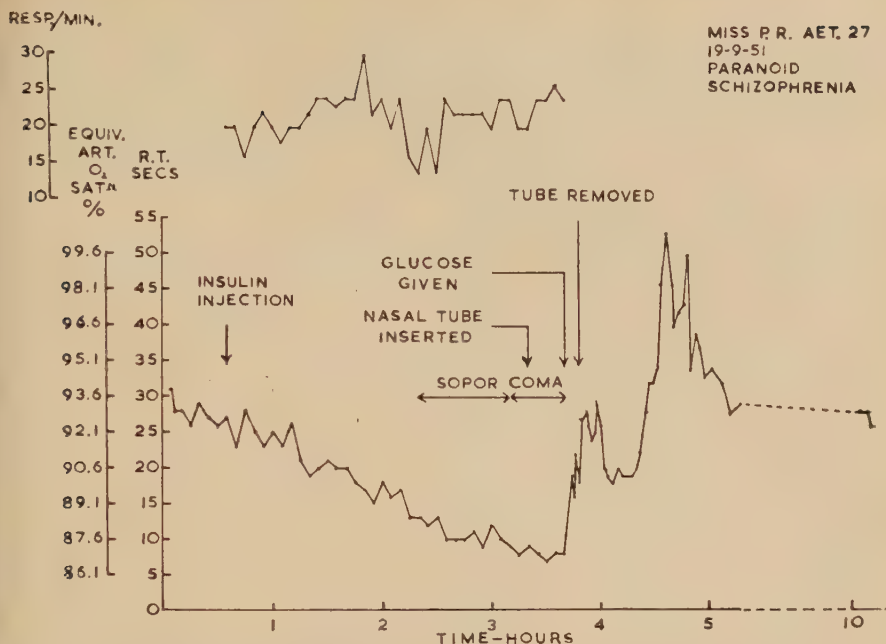


FIG. 3.—An example of the oximetric phenomena accompanying tubal interruption of insulin coma. Note the greatly increased time needed for reversal of the coma state and the stages in which recovery from anoxaemia occur.

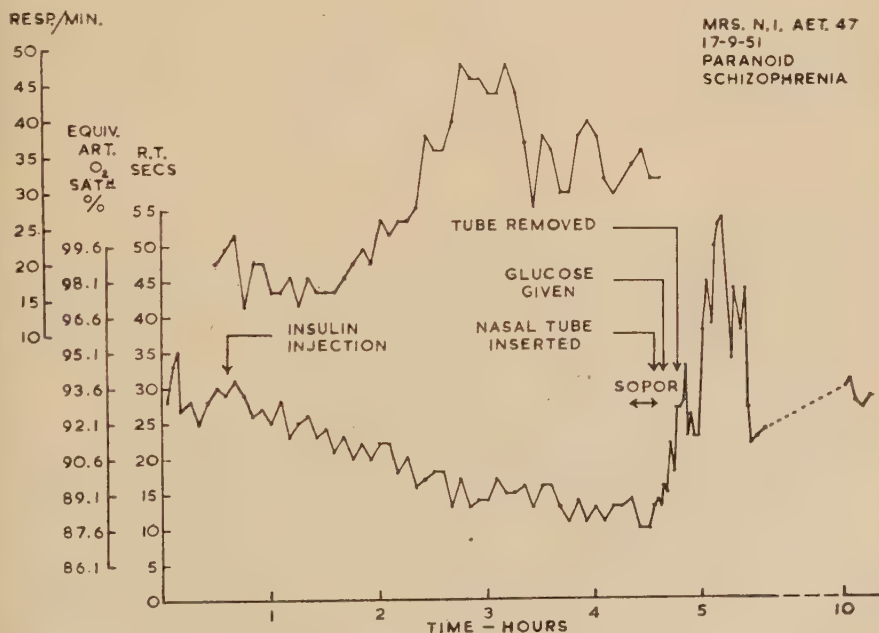


FIG. 4.—No coma ensued when this patient was given a massive injection of insulin. A possible explanation of this may be seen when her respiratory responses are compared with those exemplified in Figs. 1-3.

This Table lists the raw data on 13 schizophrenic patients who had been given insulin com-
background data, the duration of each successive phase of changing awareness, together with the
"reduction time" seconds, and converted for purposes

Patient.	Sex.	Age.	Stages reached in treatment.		Sol. insulin dose (int. units).	Phase duration (minutes).				Glucose inter- ruption.	Post inter- ruption follow- up.
			Prev. sopors.	Prev. comas.		Pre- insulin period.	Insulin to sopor.	Sopor.	Coma.		
E. A—	M.	20	3	1	280	22	112	108	18	45	137
D. C—	M.	24	38	31	160	21	153	42	33	48	202
A. W—	M.	18	7	5	400	25	150	75	25	20	125
J. Cr—	M.	31	11	9	140	22	135	42	40	30	246
A. M—	F.	33	18	13	180	14	126	70	28	20	160
M. L—	F.	26	22	20	90	32	122	47	30	67	232
V. N—	M.	30	19	18	260	20	144	38	28	52	134
J. C—	F.	24	30	24	280	26	108	90	30	44	114
D. M—	F.	39	10	10	220	34	120	60	30	48	120
H. K—	F.	19	20	17	180	32	170	50	32	42	90
J. S—	M.	26	7	4	300	34	140	24	38	50	130
P. R—	F.	27	9	9	160	30	104	50	30	98	106
N. I—	F.	47	5	2	220	34	224	12	—	60	84
Total means		28.0	15	13	220	27	132	58	30	47	145

level. Following this a negative phase of a further decline in oxygen values takes place before the values level off in an overall period of about three-quarters of an hour to reach a steady state. Follow-up observations about two and a half hours after this steady state has been attained showed little fluctuation among themselves, but the actual values reached as compared with the pre-insulin resting levels appeared of some importance. In 10 of the 12 cases whose insulin dose was sufficient to induce the coma state, these levels showed either no change, or a slight fall as compared with the pre-insulin values, but in the remaining 2 cases (Table I, patient No. 4, Mr. J. C.—, and patient No. 5, Mrs. A. M—) significantly higher values were sustained. The relevance of these changes appeared to consist in their exact correspondence with the clinical assessment of the change in mental state associated with that day's coma treatment. Where there appeared little difference between the psychiatric state of the patient on mental state examination between his resting pre-insulin period and his condition upon complete recovery following the interruption of his coma, it was also seen that no appreciable difference was found oximetrically in the measurements taken at these times. On the other hand, the two patients who showed elevations in arterial blood oxygen saturation to 97.8 per cent. and 95.7 per cent. respectively were also those who, although undoubtedly schizophrenic prior to their insulin, showed a mental state psychiatrically within normal limits during the evening of the same day.

therapy for the treatment of their disorder. Each individual protocol contains the relevant means and ranges of spectroscopic oximetric measurements recorded at five-minute intervals as convenient here into percentage arterial oxygen saturation levels.

Arterial oxygen saturation levels (per cent.)
individual means and ranges.

Pre-insulin period.	Insulin to sopor.	Sopor.	Coma.	Glucose interruption.	Post interruption follow-up.
94.2	91.8	88.2	86.1	93.6	95.4
(94.5-94.2)	(95.1-88.2)	(90.6-87.0)	(86.4-85.8)	(87.0-100.0)	(95.4-95.4)
95.4	91.2	88.2	87.6	93.6	92.1
(96.0-94.5)	(96.0-89.1)	(89.4-87.3)	(88.5-87.0)	(91.2-97.2)	(91.5-93.3)
93.0	89.1	87.0	85.5	90.3	91.5
(94.2-91.8)	(92.1-87.3)	(87.6-86.4)	(86.1-85.2)	(86.1-96.3)	(90.3-92.7)
92.4	90.0	88.8	87.6	97.5	97.8
(94.2-91.2)	(93.3-89.7)	(90.6-87.9)	(88.8-86.1)	(88.8-100.0)	(97.2-98.4)
93.6	91.2	89.7	87.6	93.0	95.7
(94.2-93.3)	(93.9-88.2)	(91.2-87.9)	(88.2-87.3)	(88.2-98.1)	(94.5-96.3)
94.2	91.5	88.5	86.7	96.6	93.0
(96.3-92.4)	(95.4-89.4)	(89.7-87.3)	(87.3-86.1)	(93.3-100.0)	(90.9-94.5)
93.0	90.9	88.2	87.3	92.7	92.7
(93.3-92.4)	(93.9-89.1)	(88.5-87.3)	(88.2-86.4)	(88.5-96.6)	(91.5-93.3)
92.1	90.3	88.5	87.0	92.4	91.5
(93.3-90.6)	(92.1-89.1)	(89.7-87.3)	(87.3-86.4)	(89.4-96.0)	(91.2-92.1)
92.1	89.7	87.3	86.7	92.7	90.9
(93.3-90.9)	(91.5-88.2)	(88.2-86.4)	(87.0-86.4)	(87.3-98.1)	(90.3-91.5)
94.5	92.1	88.8	86.7	94.8	95.1
(95.1-93.6)	(95.4-89.4)	(90.3-87.3)	(87.3-86.4)	(89.4-100.0)	(94.5-95.4)
94.2	91.2	88.8	86.7	93.6	93.3
(96.3-93.3)	(93.9-89.1)	(89.4-88.5)	(88.5-86.1)	(89.1-98.4)	(92.7-93.9)
93.0	90.9	87.9	87.0	93.3	92.7
(93.9-92.4)	(93.0-88.5)	(88.5-87.3)	(87.3-86.7)	(89.4-100.0)	(92.4-93.0)
93.3	90.3	88.2	—	93.9	93.3
(95.1-92.1)	(93.9-87.9)	(88.8-87.6)	—	(89.4-100.0)	(92.7-93.9)
93.3	90.9	88.2	86.7	93.6	93.3
(94.5-92.4)	(93.9-88.8)	(89.4-87.3)	(87.6-86.4)	(89.1-99.3)	(92.7-94.2)

The relative efficacy of intravenous as opposed to nasal tubal coma interruption is exemplified in Figs. 1 and 2, 3 and 4 respectively. It is not so much in the extent of the oximetric "rebound phenomenon" that these differences are apparent as it is in the time relationships involved. It has been noted that interruption by the intravenous method achieves a maximal oximetric elevation in a time as short as 10 to 15 minutes. With tubal interruption this time is not only extended to about 45 minutes, but also the progressive rise in oxygen values is intermittent in character and proceeds in a series of irregular phases.

The interrelationships between the peripheral arterial oxygen saturation levels and one of the important homeostatic mechanisms for maintaining them are seen in the measurements of the respiratory rate which were made simultaneously with the oximetric recordings. Figs. 1 to 4 indicate that an inverse relationship often exists between these two functional modalities. In general, as the oxygen levels progressively fall following insulin injection, so the respiratory rate shows a similar tendency to rise. Closer examination of the protocols further suggest that each major fall in the oxygen saturation values is preceded by an irregular increase in the number of respirations per minute. Changes in breathing patterns have long been noted to be associated critically with the various stages of hypoglycaemic coma and pre-coma. These variations appear meaningful when considered as homeostatic adjustments to the threat of a falling blood oxygen saturation. Fig. 4 is

especially interesting from this point of view. Patient No. 13, Mrs. N. I— (Table I), was the only subject of the total of 13 whose hypoglycaemia did not progress to coma. She was also the only patient whose respiratory rate showed a sustained and prolonged elevation above normal.

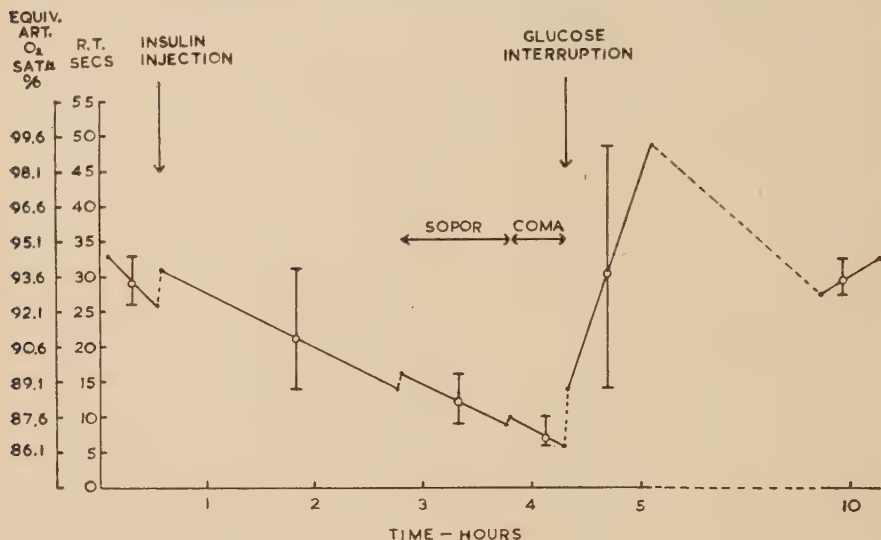


FIG. 5.—Composite chart comprising ranges and means of equivalent arterial oxygen saturation levels and time duration of each phase of treatment computed from the data on the 12 patients reaching coma. The means (open circles) and the ranges about these means (the vertical lines running through them) for the oxygen saturation levels are indicated for each phase of progressive insulin shock and its reversal. In this chart the average time in hours is given for each successive phase of treatment.

DISCUSSION.

The similarity between the symptoms of progressive hypoglycaemia and those of acute anoxia has already been alluded to. Himwich (1951, p. 273) emphasizes that not only is the resemblance seen in their nature but also in the order of their appearance, and he speaks (p. 276) of the "dissolution" of the brain under the dissection scalpels of hypoglycaemia and anoxia." The essential identity of these conditions is further exemplified in other physiological concomitants of anoxia which have been observed also during insulin shock. Thus, an increase in the erythrocyte count and in the haemoglobin level have been noted (Georgi, 1939; Beiglbock and Dussik, 1938); likewise an increase in blood adrenaline values (Tietz *et al.*, 1940); characteristic changes such as flattening and inversion of the T wave and widening of the QRS complex in the E.K.G. (Messinger, 1938; Bellet *et al.*, 1939; Hadorn, 1937; Beiglbock and Dussik, 1938), and in the E.E.G., similarly, depression in the dominant alpha rhythms with an increase in theta components (Hoagland *et al.*, 1937*a* and *b*; Himwich, Hadidian *et al.*, 1939). So far as changes in consciousness are concerned, it has already been pointed out that these show a striking parallelism both with falling oxygen levels and with progressive hypoglycaemia. The inter-dependence of these three differentials of awareness, blood oxygen and blood glucose is clearly demonstrated in our protocols by the time relationships involved in the absorption of the ingested glucose, as opposed to the immediate effects of glucose administered by the intravenous route. Increasing awareness was a slow, irregular and intermittent recapitulation in reverse of the consciousness thresholds influenced by hypoglycaemia when a tubal method of interruption was employed: it was rapid and continuous when glucose was exhibited intravenously. These two patterns of awakening resembled closely those seen when similar correlations between changing thresholds of consciousness and

oximetric measurements were studied in natural sleep (Lovett Doust and Schneider, 1952). Here the time relationships involved in awakening could either approach those of the gradual descent into sleep or be compressed into a matter of minutes.

Many theories concerning the mechanism of action of deep insulin coma have been put forward in the past. They may be conveniently divided into five principal groups, depending on the main interests of the investigator. These groups include hypotheses regarding autonomic nervous system imbalance, Gellhorn (1938), for example, feeling that insulin corrects the sympathetic-adrenaline hypofunction he has emphasized as characteristic of schizophrenia. The effects of insulin on the cerebral circulation (Baruk *et al.*, 1945) leading to changes in the diameter of pial vessels; the influence of insulin on various cerebral enzyme systems (Hoskins, 1946); the effects of the hormone on the neuro-endocrine imbalance demonstrated by several workers (Hoskins, 1946; Hoagland *et al.*, 1946; Parsons *et al.*, 1949); and the concept of insulin as a growth hormone (Schneider, 1949) comprise many of the theories. It is not, however, with possible theories of action *per se* so much as with a mechanism effect coincident with the interruption of coma that we shall finally concern ourselves.

Gerard (1938) considered that one of the most important effects of insulin treatment lay in the "rebound phenomenon" which led to an increase in the respiration of the brain. This phenomenon was seen as a constant feature in the investigations reported in this paper. Consistently the arterial oxygen saturation levels following coma rose to values well above the pre-insulin resting levels when glucose was administered. It is with the degree and duration of this rebound that the immediate oximetric and clinical prognosis in an individual case appears to be associated. This finding, poorly brought out in the literature, would seem to the writers of some practical importance with regard to the relative efficiency of treatment in psychiatry. If, as has been suggested to be the case (Lovett Doust, 1951a), a close association exists between the height of blood-oxygen values and the occurrence of psychiatric symptoms, then a therapy capable of producing a rise in oxygen values is efficient with respect to the intensity and duration of that rise. It is important to point out, however, that a rise in values unrelated to a previous period of stress has no duration apart from the agency causing it. Thus it can readily be observed that profound changes in the psychiatric status of a patient take place with the inhalation of pure oxygen; such changes are reversed quickly following the cessation of such inhalation. Given the preliminary period of anoxaemic stress, however, as in insulin shock therapy, the homeostatic adjustment to such stress, or "rebound phenomenon," induces a rise in the oximetric levels which is maintained, at least in part, in relationship to the degree and duration that the stress has been allowed to act.

SUMMARY.

1. The arterial blood oxygen saturation levels of 13 schizophrenic patients have been followed oximetrically, and their respiratory rates counted, during the course of their treatment by insulin shock therapy. Coma was reached by 12 of the patients; hypoglycaemia was interrupted by intravenous glucose in 11 and by nasal tube in 2 patients.

2. Peripheral spectroscopic oximetry, with measurements taken every 5 minutes over the course of 8 to 10 hours in each patient, showed that the findings in minute vessels of the finger-nail fold paralleled those of other workers using arterio-venous difference methods. A progressive and profound anoxaemia ensued following the injection of insulin in massive doses.

3. Mean oxygen resting levels of 93.3 per cent. fell progressively to reach 88.2 per cent. in sopor and 86.7 per cent. in coma. Glucose interruption was accompanied by a rapid rise to 99.3 per cent. oxygen ("rebound phenomenon"), after which the maximal values fell off until a steady state was attained. In 2 patients who showed clinical improvement in their psychiatric state following the day's treatment, the final oxygen saturation levels were considerably higher than their resting levels (93.0 rising to 96.9 per cent.). No significant difference between pre-insulin and post-interruption final steady state oxygen values was observed in the 11 patients who showed no psychiatric improvement (93.6 as against 93.0 per cent. respectively).

4. It is noted that blood oxygen saturation values, as measured oximetrically, bore a striking correspondence with the differential levels of awareness reached

during progressive insulin hypoglycemia. Insidious clouding of consciousness, the stages of sopor and of coma and the reversal of these changing thresholds could all be accurately predicted in terms of oximetric values; correlation with independent and experienced clinical judgment was high.

5. The homeostatic significance of changing respiratory rates as an adjustment to the treat of insipient deepening anoxaemia is discussed and the function of the "rebound phenomenon" as an indicator of stress response is suggested.

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THE EFFECT OF ELECTRICAL STIMULATION OF THE BRAIN ON THE PERCEPTION OF PAIN.

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THE fact that electrical stimulation of the brain can produce unconsciousness in man and animals has been known since the eighteenth century, and from time to time this knowledge has been used in the production of anaesthesia for surgical purposes; Hobday, in 1932, performed castrations and herniotomies in small animals under electrical general anaesthesia, and in 1935 Hertz used electrical anaesthesia for laparotomies in dogs. To-day electrical stunning is used in bacon factories with the object of rendering pigs unconscious before slaughter. Electro-convulsant therapy (E.C.T.) is widely used in mental hospitals for the treatment of certain conditions, and recently Freeman (1948) has modified this technique to produce surgical anaesthesia for prefrontal leucotomy.

In some instances electrical anaesthesia has proved satisfactory, but there have been reports of "distorted consciousness" after E.C.T. in human subjects (Morgan, 1950), and of electrical curarization after industrial accidents (Hume, 1935); in these conditions the subject is conscious of sensation but unable to make voluntary movements. Such a condition is only appreciated when the subject is questioned after regaining full consciousness, and hence, if it occurred in animals, it would not be readily recognized.

The object of the work described in this paper was to determine the effect of the many variables of electric stimulation, and to investigate the state of consciousness of human subjects and animals after electric stunning. It was hoped thus to provide a basis for future work on electrical anaesthesia and to acquire a better understanding of the action of E.C.T.

EXPERIMENTAL PROCEDURE.

Material.—The material consisted principally of rabbits of both sexes of various breeds and ages, ranging in body weight from 200 gm. to 2,000 gm. A small group of mental hospital patients was observed before and after routine E.C.T.; pigs and sheep were observed during the normal electrical stunning prior to slaughter.

Apparatus.—Electro-corticograms and electro-cardiograms were recorded as described in the previous paper (Croft, 1952). Electrical stimulation for rabbits was by means of a square-wave stimulator, designed to provide constant current (Bernstein, 1950). The following could be independently varied: frequency 1–1,000 cyc./sec.; pulse width 0.1–50 m.sec.; amperage 0–80 mA. Pigs and sheep were stunned by 50 cyc./sec. mains A.C. transformed down to 70–90 V. Human E.C.T. was given with 50 cyc./sec. A.C. transformed down to 90–100 V.

RESULTS.

The results will be described under two main headings:

- (i) Effect of variables on the production of unconsciousness.
- (ii) State of consciousness after electric stimulation.

Effect of Variables.

The typical sequence of events following effective electrical stimulation was as follows:

(1) Initial momentary flexion of the hindlegs, followed by violent extension; the forelegs were stiff at this stage, but all reactions in the forelimbs were less extreme. The spine was rigid, and the head strongly flexed backwards. Respiration was arrested and defaecation and urination commonly occurred. 0–10 sec.

(2) Rigidity passed off gradually, and weak clonic contractions of all limbs occurred. 10–30 sec.

- (3) Respiration re-started and the animal became flaccid. 30-60 sec.
- (4) Muscular tone normal, but animal lay motionless. Up to 8 min.

The above times refer to the rabbit, but the essential features of the four stages were similar in rat, pig, sheep and man, and in rats undergoing Metrazol convulsions. The extensor tonus of the first stage always occurred when the stimulation was sufficient to cause unconsciousness and could safely be used as an indicator for this purpose. When stimulation was inadequate (i.e. did not cause unconsciousness) one or more of the other stages might be seen, but extensor tonus was not present. In this work stimulation which was followed by extensor tonus is described as "effective," and a shock which did not produce extensor tonus is referred to as a "missed shock."

The following variables were studied with reference to the rabbit: Amperage, frequency, pulse width, time and site of application, breed and sex. Twelve animals were used for studying each variable, and when a critical value was found it was re-determined several times on the same animal over a period of a month, and on a random sample of animals.

Amperage.—This was a factor of great importance. A threshold value of 25-30 mA. was essential for effective stimulation; if the current was below this value, no alterations in the other variables caused stunning. Between 30 and 80 mA. there was little difference in the effect produced.

Frequency.—At 25 cyc./sec. or less a true fit did not occur, but the animal twitched synchronously with the stimulus; 50 cyc./sec. and upwards produced unconsciousness (provided that the other variables were correct), 100 cyc./sec. being slightly more effective than 50 or 200 cyc./sec. Higher frequencies, up to 1,000 cyc./sec., seemed to cause pain as the current was switched on, and were no more effective in causing unconsciousness.

Pulse width.—Pulse widths below 1 mS. did not usually cause unconsciousness, but 2 mS. was very effective and pulses up to 50 mS. could be used satisfactorily.

Time of application.—Provided that the time was at least 2 sec., further increases did not make any appreciable difference to the results. It was *not* possible to compensate for low current strength by increasing the time of application.

Site of application.—The most effective site was (ii), which was in the region of the motor cortex; true fits could be produced by stimulation at (i) and (iii), points 1 cm. anterior and posterior to (ii), but a greater current strength was needed than at (ii).

State of Consciousness after Electric Stimulation.

The state of consciousness was investigated by a number of different tests, and the general behaviour of the animal or human subject was also carefully observed. The tests used were:

- (i) Reaction of the pupil to light.
- (ii) Cardiac pain reflex (Croft, 1952).
- (iii) E.E.G. in human subjects, electro-corticogram in animals.
- (iv) Paw retraction reflex.

The normal conscious electro-corticogram from the precentral granular area of the rabbit's cortex had a characteristic frequency of 5-8 cyc./sec.; from other parts of the cortex the rhythms were less regular, but they always contained a large proportion of fast rhythms; slow rhythms (1-3 cyc./sec.) were only seen in pathological conditions or during anaesthesia.

E.Co.G. recordings could be made 1 second after switching off the current used for stimulating the rabbit. During the phase of extensor tonus bursts of high-frequency activity alternated with very slow high-voltage waves; the record did not change appreciably until the end of the clonic contractions, when it flattened out completely; 1-3 minutes after stimulation this flat record changed, and slow waves of varying voltage appeared. The normal high-frequency E.Co.G. was not usually seen until at least 5 minutes after the stimulation and then only intermittently; at this time the frequency was often slightly below the normal one (4-6 cyc./sec.). In some experiments no high frequencies appeared until 8 minutes after stimulation, but in every case the normal 6-8 cyc./sec. rhythm was well-established after 20-60 minutes, and the E.Co.G. was then indistinguishable from the pre-ictal one of the same animal.

Several interesting phenomena occurred in the post-ictal E.Co.G. of the rabbit, and they may be considered under the following headings: (i) spike and wave records; (ii) high-frequency bursts; (iii) phase reversal.

(i) Spike and wave records were seen at intervals varying from 1-8 minutes after stimulation; the frequency was always 2-3 cyc./sec. and the activity lasted 20-60 seconds, being followed in most cases by a short period of electrical silence. The record appeared simultaneously in all leads and was in phase.

(ii) Bursts of high-frequency waves of large amplitude occurred at intervals varying from 1-17 minutes after stimulation, and lasted typically for 4-10 seconds. They were normally present on only one channel, though occasionally there was a

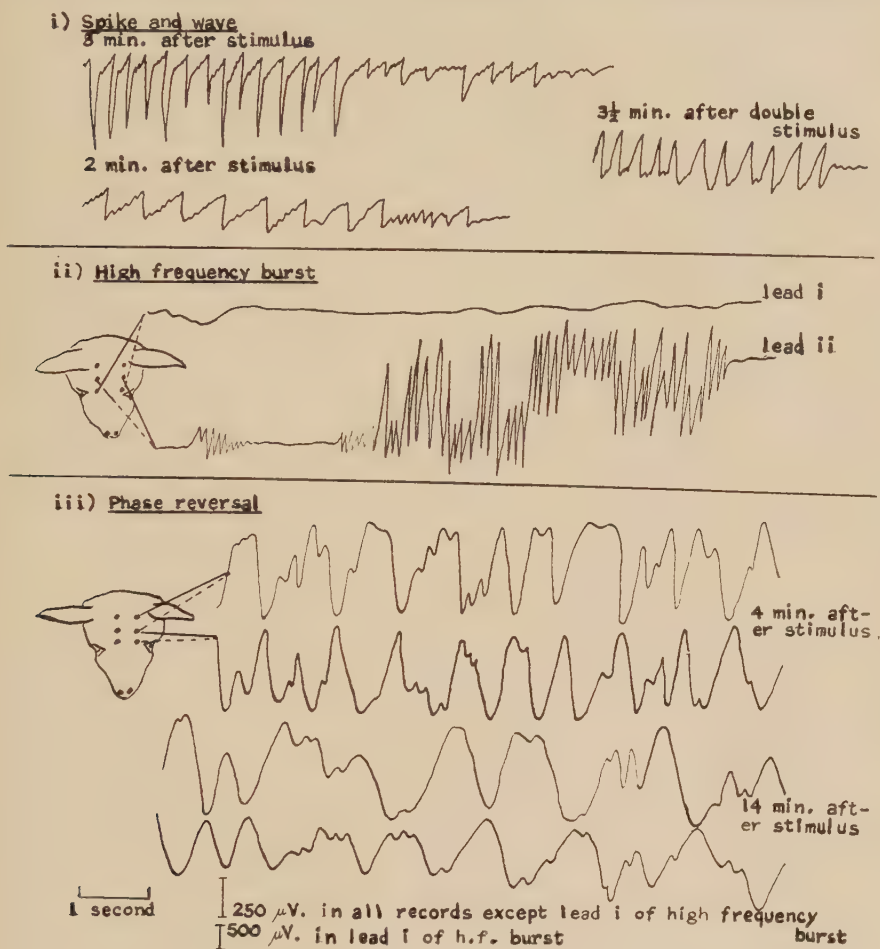


FIG. 1.—Electro-corticograms from rabbit after electro-convulsant stimulation.

slow spread over the cortex. This record also was usually followed by a short period of electrical silence. The bursts were recorded from positions (i) and (ii) and bore no relation to the electrodes used for stimulation, appearing sometimes from the same pair and sometimes from a different pair.

(iii) Phase reversal was less common after stimulation than the two previous types of record, but it was clearly shown in four different rabbits. It appeared between 3 and 7 minutes after stimulation and lasted for 5-6 minutes (Fig. 1).

E.Co.G. records after missed shock showed none of the characteristics of the post-ictal record of effective stimulation; they were essentially similar to the normal records.

The general picture of the human E.E.G. after electro-convulsant therapy was comparable with that of the rabbit, but the time intervals were much longer. During the first 10 minutes the record consisted mainly of δ -rhythm, which was usually out of phase in any two channels with a common electrode on the central part of the scalp; the subject was unconscious at this stage. The δ -rhythm was gradually replaced by bursts of faster frequencies, and the subject opened his eyes and made unco-ordinated movements, but did not seem to recognize his surroundings; 30-45 minutes after the E.C.T. the α -rhythm reappeared and the patient gave intelligent answers to questions. The spike and wave and other phenomena seen in the post-ictal records of some rabbits were not seen in human E.E.Gs., but between 10 and 20 minutes after E.C.T. the human records often showed long bursts of θ -rhythm (7 cyc./sec.), which were not seen in the normal record of the same individual; the phase relations of this rhythm indicated that it had a sub-cortical origin, probably in the diencephalon.

The reaction of the pupil to light can be used as an indicator of the activity of the brain at the level of the Edinger-Westphal nucleus. Preliminary animal experiments showed that this reflex reappeared before the cardiac pain reflex, after elimination of both by electric stimulation. The cardiac pain reflex was positive at a time when the animal made no voluntary muscular movement and did not respond positively to the paw retraction reflex, and when on casual inspection it would be considered unconscious.

As the time intervals between the various phases of the recovery period were very short, double shocks were given to a few animals to extend these phases (Klein and Early, 1949). The reflexes reappeared in the same order in these animals, thus confirming the previous results. The overall picture of the levels of consciousness in the period following electric stimulation is best shown by means of a table (Table I).

One other point which was noted in many of the experiments was the appearance, in the rabbit, of a hypersensitive phase, lasting 2-5 minutes and occurring about 8 minutes after stimulation. The cardiac pain response was exaggerated during this period, and any slight noise caused extreme alarm and violent escape movements; the E.Co.G. was usually normal during this stage, but occasionally bursts of high-voltage spike discharge occurred in one channel.

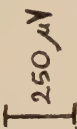
DISCUSSION.

There are numerous references in the literature to the effect of variations in the electrical characters of the stimulation required to produce an epileptiform fit in man and animals (Ivy and Barry, 1932; Clark and Wall, 1934; Harreveld *et al.*, 1943; Gaultierotti *et al.*, 1949; Pierce, Russell and Patton, 1950), and Davenport and Davenport (1948) have studied the effect of variations in the condition of the experimental subject. Gaultierotti *et al.* (1949) used a frequency of 280 cyc./sec. and considered that this was a critical value; other workers, however, have used a wide range (30-300 cyc./sec.) and found that frequency has little effect on the convulsion, provided that it is not less than 50 cyc./sec. (Harreveld *et al.*, 1943; Arief, 1949). The experiments described in this paper confirm the latter view, but both the species of experimental animal and the method of stimulation differ from that of Gaultierotti *et al.* Walter's work on photic stimulation (1951) indicates that in certain circumstances the frequency of the stimulation can be extremely important, but it is obvious from the present series of experiments that reasonable variations in frequency have little effect on the production of unconsciousness by electrical means.

Strength-duration curves are a characteristic of nervous tissue, and do apply to electrical stimulation if the time of application of the stimulus is of the order of a fraction of a second (Toman and Goodman, 1947); in this connection Longley (1950) has stated that at least two complete electrical cycles must pass if a convulsion is to be produced, so that if the frequency is 50 cyc./sec. the current must pass for a minimum period of 40 mS. When the stimulus is applied for one second or longer the relation no longer holds; the brain cells give an initial maximal response, and are then in a refractory state when further stimulation is ineffective. Russell (1948) and Boshes *et al.* (1943) note that the pattern of the fit is affected by neither intensity nor duration of the stimulus, provided this exceeds the threshold value.

Variation in the electrical pulse width has surprisingly little effect on the response provided that it is at least 1 mS. (below this width, the wave form is not truly

TABLE I.—*Changes in Activity of C.N.S. of Rabbit after Electro-convulsant Stimulation.*

Time after stimulation (minutes)	Cardiac pain reflex		Paw reflex	Voluntary movements	Electro-corticogram
	Per cent. increase with stimulation;	Duration of response (sec.)			
Before stimulation	12	7	Normal	Normal	
2	—	—	—	—	
5	1	70	—	—	
7	6	70	—	—	
9	5	70	Very slow	—	
17	5	70	Slow	—	
25	7	30	Slow	Slight	
120	8	12	Normal	Normal	 1 second  250 μV

ing at the thalamic level, but in which connections between thalamus and cortex are impaired. These connections, being relatively recent from the evolutionary point of view, are likely to be more sensitive to submaximal stimuli, and to recover more slowly from an effective electric stimulus.

Roth (1951) has suggested that E.C.T. in man affects particularly a mid-line diencephalic structure with access to all cortical structures, and especially to the frontal lobes, and that this may be homologous with the thalamic reticular system of animals discussed by Dempsey and Morison (1942) and others. Roth believes that by abolishing the activity of the higher, recently developed parts of the brain homeostatic influence of the lower centres can be asserted and the subject may thus regain a more stable equilibrium. Russell (1948) has shown that E.C.T. eliminates first the habits which have been most recently learned in animals that have undergone a long course of instruction. Theories such as these may explain in part the therapeutic value of E.C.T., and they fit in well with the experimental results described in this paper. These results do, however, also show that electro-convulsant stimulation is essentially a stunning process; the cortical neurons are stimulated maximally, and are then in a totally refractory state for some time. The post-ictal spike discharges indicate the risk of brain damage during electrical stimulation, and numerous observations on memory changes after E.C.T. show that its effect on function can be drastic. Recent work by Holzbauer *et al.* (1952) has demonstrated that electro-convulsant stimulation seriously retards growth and healing in animals. These long-term results, together with the abnormal reflex reactions in the immediate post-ictal period, show that there are many varied factors to be considered in the future development of electro-convulsant stimulation for therapeutic and anaesthetic purposes.

SUMMARY.

- (1) The influence of a series of electrical and biological variables on the efficiency of electrical stunning has been investigated.
- (2) The state of consciousness following electrical stimulation has been examined by a battery of tests, including the E.E.G.
- (3) The implications of the unusual states shown by these tests are discussed.

ACKNOWLEDGMENTS.

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THE ASSESSMENT OF PAIN PERCEPTION.

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THE assessment of pain perception is a subject of great importance from both the practical and the theoretical aspect. The increasing use of curare-like drugs as muscular relaxants and basal anaesthetics (Mushin, 1951), and in conjunction with electro-convulsant therapy (E.C.T.), has made the orthodox tests for depth of anaesthesia unreliable because they depend on the activity of voluntary muscle. E.C.T. itself (Morgan, 1950) and industrial electrical accidents (Hume, 1935) have given rise to unusual states of consciousness which cannot be fully understood until more is known about the way in which electric shock affects the central nervous system. On the theoretical side many explanations of the essential features of a state of consciousness have been given, but none of them accounts completely for all the observed phenomena; investigations designed to improve methods of assessment should provide useful information which, when correlated with that from other fields, may ultimately lead to a better understanding of the conscious state. The object of the experiments described in this paper has been the development of tests which will indicate the level of consciousness, and in particular the appreciation of pain, when the voluntary muscles are paralysed.

EXPERIMENTAL METHODS.

Material.—The material consisted of—

- (i) Rabbits of both sexes of various breeds and ages, ranging in body weight from 800 gm. to 2,000 gm.
- (ii) Six normal male human subjects; 5 mental hospital patients, male and female, classified as depressive.

Apparatus.—Electro-cortigrams (E.Co.G.) were recorded on a 6-channel Mitchell E.E.G. machine and on a Marconi 4-channel machine; heart rates were recorded by taking electro-cardiograms on one channel of the E.E.G. machine. The electrodes for the animal E.Co.Gs. consisted of fine stainless steel pins driven through a cork support and the skull of the anaesthetized animal so that the tips of the pins were in contact with the cortex. The penetration of the pin was checked *in vivo* by X-ray, and post-mortem by histological methods (Marshall, 1940). If the cork support was sutured to the skin over the skull, the electrodes could be left in position for several days without apparent discomfort (Fig. 2). These electrodes were used for E.Co.G. recordings and for stimulation; they were connected to the required leads by crocodile clips. Three standard positions were used, the external landmarks being—

- (i) the level of the posterior canthus of the eyes;
- (ii) midway between (i) and the anterior border of the base of the ear;
- (iii) the level of the anterior border of the base of the ear.

Hypodermic needles were used as electrodes for recording the animal electro-cardiograms; they were placed subcutaneously, one over the heart and the other over the lumbar vertebrae (or on any other accessible "indifferent" site).

The electrodes for the human E.E.Gs. were the usual Marconi scalp type, and were placed on the occipital and parietal areas. Human electrocardiograms were recorded on the E.E.G. machine with scalp electrodes placed over the heart and on the left arm.

The stimulator used for the rabbit experiments was modelled on that described by Bernstein (1950) and was designed to provide a constant current and square wave pulses. The pain stimulus for the rabbit was a pin-prick on the nose, and in the experiments with human subjects 0.1 ml. distilled water was injected intradermally on the forearm.

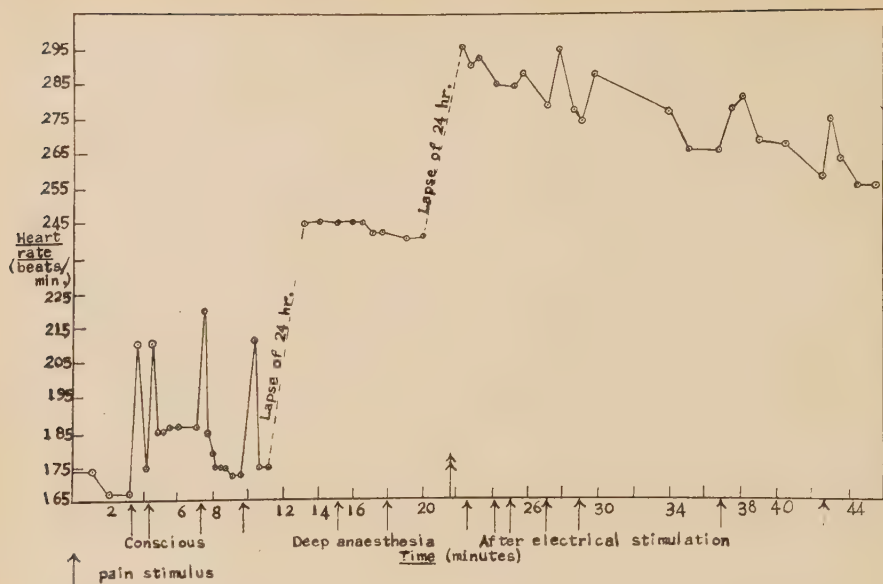


FIG. 1.—Arrangement of electrodes for rabbit recordings and stimulation.

RESULTS.

The results will be described under two main headings :

- (1) Determination of sensitivity to pain by the cardiac pain reflex (c.p.r.).
- (2) Assessment of level of consciousness by E.Co.G. and E.E.G.

Determination of Sensitivity to Pain by Cardiac Pain Reflex.

In order to assess the awareness of the animal under these conditions it was necessary to use involuntary muscle, under cerebro-cortical control, the activity of which could be easily recorded. Longley suggested that the cardiac muscle fulfilled these conditions, and the electro-cardiogram was recorded on the E.E.G. machine concurrently with the E.E.G. itself.

The normal heart-rate of the rabbit varies from 190–290 beats/minute, but in any particular animal the resting rate only varies by 1–2 per cent. from the mean value. When the conscious animal felt pain, in the form of a pin-prick on the nose, the heart-rate increased by 20–30 per cent.; typically the increase lasted about 15 seconds, after which the rate quickly returned to the resting level, or to a subnormal level for a few seconds. The response always occurred and its magnitude was fairly constant in any one animal, varying little with the strength of the stimulus. When the animal was deeply anaesthetized the response was completely abolished, and in states of light anaesthesia it was reduced in magnitude, and the return to normal was slower (Fig. 2). The cardiac pain reflex behaved similarly in human subjects tested in the conscious state and at various levels of ether anaesthesia.

In the rabbit, immediately after an electrical convulsion, the c.p.r. was absent, and the stage at which it could first be elicited is shown in Table I. The reflex invariably appeared before the paw retraction reflex, and was in fact present at a time when the animal would normally be considered unconscious; voluntary movements appeared some minutes later (Table I). In human subjects there was a stage, just before consciousness was lost, when the c.p.r. was positive but no other external indication of pain perception was given; subsequent interrogation revealed that the subject felt the stimulus, but “had no energy to signal.”

Assessment of Level of Consciousness by E.Co.G. and E.E.G.

The normal conscious E.Co.G. from the precentral granular area of the rabbit cortex has a characteristic 5–8 cyc./sec. rhythm, while that from other parts of

TABLE I.—*Reappearance of Reflexes after Electro-convulsant Stimulation (Rabbit).*

No.	Conscious.	Per cent. increase in heart rate.	Cardiac pain reflex. After electrical stimulation.		Paw reflex.
			Time when first seen (minutes after stimulation).	Per cent. increase in heart rate at this time.	Time when first seen (minutes after stimulation).
1	.	11	2 $\frac{1}{4}$	7	6
2	.	26	3	4	6
3	.	40	2	6	4
4	.	10	2 $\frac{1}{2}$	5	7
5	.	11	5	1	9
6	.	—	3	4	5
7	.	25	4	13	
8	.	6	5	2	
9	.	15	4	7	
10	.	12	5	7	
11	.	12	5	10	
12	.	—	4	10	

The c.p.r. was tested every minute in all experiments until a positive response occurred. The paw reflex was not timed accurately in rabbits 7-12, but it was never present at the time when the c.p.r. appeared.

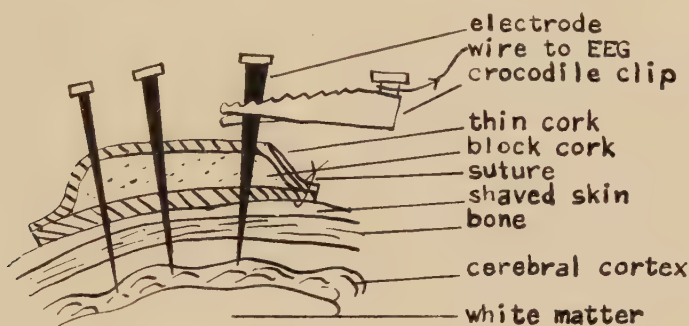


FIG. 2.—Effect of pain stimulus on rabbit heart rate under different conditions.

the cortex is less regular, but always contains a high proportion of fast rhythms; slow frequencies, as in man, are indicative of decreased cortical activity, or of a pathological condition. A number of E.Co.Gs. of rabbits in different stages of Nembutal and Pentothal anaesthesia were taken, and the changes in the record agreed reasonably well with the observed state of the animal.

In the human subject the α -rhythm was recorded while the depth of ether anaesthesia was gradually increased. The percentage of E.E.G. record showing no α -rhythm was calculated for each 20-second period, and a sharp rise in this percentage occurred, as unconsciousness supervened, in every one of six subjects tested (Fig. 3).

E.Co.G. recordings could be made 1 second after switching off the current used for electric shock in the rabbit. At the end of the clonic phase of the convulsion, when the rabbit was lying in a relaxed state, the E.Co.G. was completely flat; 1-3 minutes after stimulation slow δ -waves of varying voltage appeared. The normal high-frequency E.Co.G. was not usually seen until at least 5 minutes after the shock, and then only intermittently; the frequency was often slightly lower than normal at this stage (4-6 cyc./sec.). In some animals no high frequencies appeared until 8 minutes after stimulation, but in every experiment the normal 6-8 cyc./sec. rhythm was well established between 20 and 60 minutes after stimulation; the record was then indistinguishable from the pre-ictal one of the same animal.

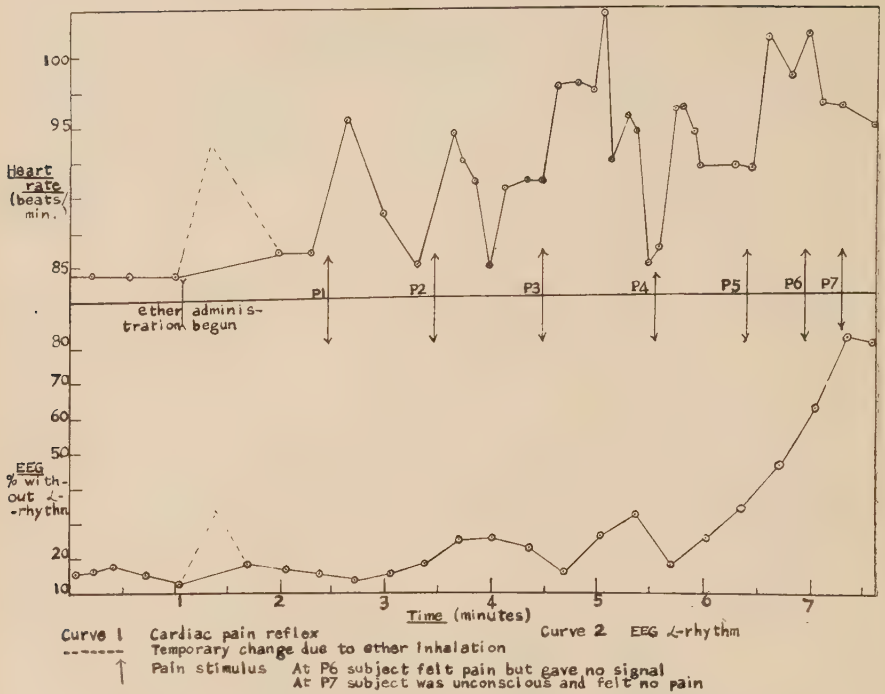


FIG. 3.—Effect of anaesthesia on cardiac pain reflex and E.E.G. in man.

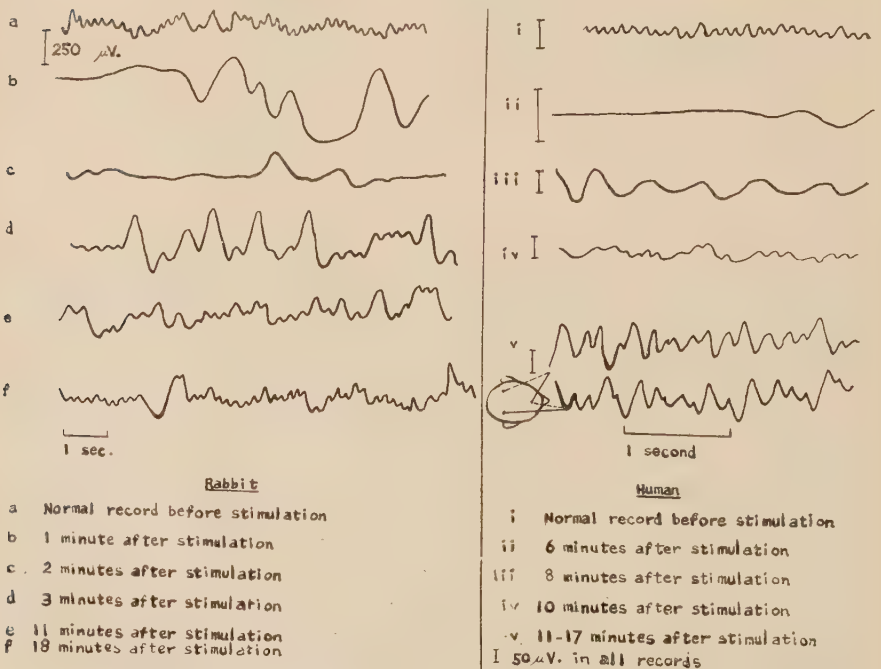


FIG. 4.—Effect of electro-convulsant stimulation on rabbit E.C.G. and human E.E.G.

Comparable changes occurred in human E.E.Gs. after electro-convulsant therapy, but the time intervals were longer than in the rabbit E.Co.Gs. The record consisted mainly of δ -rhythm for the first 10 minutes after E.C.T., and the patient appeared quite unconscious during this period; the δ -rhythm was then gradually replaced by bursts of faster frequencies, and the patient opened his eyes and made unco-ordinated movements, but did not recognize the people round him. Between 10 and 20 minutes after E.C.T. the E.E.G. often showed long bursts of θ -rhythm (7 cyc./sec.); the phase relations of this rhythm indicated that it had a sub-cortical origin, probably in the diencephalon. α -rhythm reappeared 30-45 minutes after E.C.T. and the patient's responses to questions and commands were normal at this time (Fig. 4).

DISCUSSION.

Experiments showed that the cardiac pain reflex could safely be used as an indicator of consciousness of pain in human and animal subjects, and since it did not involve voluntary muscle, it was valid during states of curarization. The exact regions of the brain involved in this reflex are not known; the afferent impulse travels by the lateral spino-thalamic tract to the ventral part of the lateral thalamic nucleus, and the efferent path is from the cortex to the vaso-motor centre in the medulla. The association area between the afferent and efferent sides is uncertain, but when the reflex is positive, part at least of the thalamus and the cortex must be functional.

After electric shock in the rabbit there is definitely a short period when the c.p.r. is positive whilst the paw reflex is still absent, and a comparable condition has been noted by Hume (1935) in man after electrical accidents. Voluntary muscle apparently cannot function as the final link in a reflex at this stage, and the existence of this condition, when pain can be appreciated but voluntary movement cannot be made, is a factor which should be considered in future work on electrical anaesthesia.

There is abundant evidence that the E.E.G. and the state of consciousness are closely linked (Lowenbach and Lyman, 1940; Martin, 1949; Brazier, 1948; Gibbs, Davis and Lennox, 1935; Swank and Foley, 1948; Adrian, 1947), and Bickford (1950, 1951) has actually devised an apparatus in which the summated cortical potentials operate the plunger of a syringe containing an anesthetic solution, so that any desired level of anaesthesia can be automatically maintained. Faulconer, Pender and Bickford (1949) found that the α -rhythm of man was a good guide to the state of consciousness during the induction and recovery stages of anaesthesia. Lewy and Gammon (1940) have described a 5 cyc./sec. rhythm as the α -rhythm of the rabbit; in the experiments described in this paper the constant rhythm was a 6-8 cyc./sec. one, and although it did not arise from a part of the cortex comparable with that which gives rise to the α -rhythm in man, it was an equally good indicator of the state of consciousness during chemical anaesthesia, and was therefore carefully studied in the E.Co.G. after electrical stimulation.

The E.E.G. of both man and rabbit was flat at the end of the clonic phase following electro-convulsive shock, but after a short period δ -waves appeared; these waves are generally considered to have a sub-cortical origin, and hence their appearance on the cortex indicates that the cortex itself is inactive. Walter (1936) has noticed the widespread appearance of δ -waves simultaneously with loss of consciousness in man, and Lennox *et al.* (1951) associated the appearance of δ -waves in monkey E.E.Gs. with a condition of stupor.

After this stuporose stage the δ -rhythm is interrupted by bursts of faster rhythm, and therefore, presumably, the cortex is becoming active again. The cardiac pain reflex is positive at this stage but there is paralysis of voluntary muscle; it appears that only certain parts of the cortex have recovered their function. Jewsbury (1951) considers that perception of pain *can* be performed by large areas of the cortex, and it can thus occur when recovery from electric stimulation is incomplete.

Finally, normal α -rhythm is re-established indicating that the cortex is fully integrated with sub-cortical structures, and at this stage the subject has regained control of the voluntary muscles. Thus, the results indicate that the cardiac pain reflex is a reliable and convenient method of assessing pain perception, and that it is particularly useful in conditions of curarization when the voluntary muscles are paralysed by electrical or chemical means.

SUMMARY.

(1) A reflex is described by means of which pain perception in man and animals can be assessed when voluntary musculature is paralysed.

(2) Rabbit E.Co.Gs. and human E.E.Gs. in various stages of anaesthesia and after electro-convulsant shock are described.

(3) The functional activity of the brain responsible for the observed records is discussed.

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A PRELIMINARY REPORT ON FATIGUE AND PAIN TOLERANCE IN DEPRESSIVE AND PSYCHONEUROTIC PATIENTS.

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PAIN and fatigue, subjectively experienced, are two of the commonest complaints made by patients suffering from a variety of psychoneurotic and psychotic disorders. Neither phenomenon has so far been adequately studied with the available objective techniques, and the present paper embodies results of preliminary experimental investigations of fatigue and pain tolerance, together with a review of some of the clinical aspects of the problem.

In psychiatric disorders pain rarely produces overt signs which allow the observer to judge its severity, and the excruciating pain complained of by some patients appears to be accompanied by much less emotional reaction than, for example, the pain experienced by the normal individual after a burn, a crushed finger, or an abdominal catastrophe.

Fatigue is even less susceptible to assessment, and the patient's description of his experience does not necessarily represent at all accurately the degree of his fatigability. Complaints of fatigue may represent lack of interest in the task, mental preoccupation with something else, or inability to exert oneself, adduced as fatigue, but unaccompanied by the disagreeable physical sensations normally associated with it. It is not known to what extent an emotional disturbance, through the physiological upset it creates, makes for greater inefficiency and therefore more rapid fatigability in co-ordinating muscular movements and performing tasks. Great discrepancies between performance and complaints of fatigue are observed in different mental conditions, and it is a commonplace that the normal individual who complains of real fatigue, mental and physical, when performing an uninteresting task, presents exactly the opposite picture, objectively and subjectively, when doing something agreeable immediately afterwards.

Clinically, intolerance of pain is observed in tense, anxious individuals, who show an alertness and quickness of response, accompanied by an unpleasant subjective hypersensitivity to all sorts of external stimuli—noise, light, touch, and so forth. These patients tend also to have little perseverance, and complain quickly of fatigue.

Neurasthenics, hysterics and various psychoneurotic patients may complain of being tired, and in their performance show little application and appear genuinely to be highly fatigable. They may, however, show no particular intolerance of external stimulation, and in fact may give an appearance of calm and indifference.

In the true endogenous depressive, the earliest complaint is of a general slowing-up of activity, accompanied by a sense of effort and a subjective sense of fatigue. Provided the depression is not very great, these patients show a high degree of perseverance, and in clinical practice one finds, for example, that a housewife will persevere with her complete day's work, even though it demands enormous effort and takes very much longer to do than normally. These patients also show disregard for external stimulation, and particularly pain. They may neglect discomfort, cold and hunger, and in their suicidal attempts they seem to be indifferent to the suffering one would expect them to experience.

In patients suffering from reactive, involutional or agitated depression the personality is usually different, and we do not regard these as belonging to the typical manic-depressive form of psychosis. By comparison with the manic-depressive group, they tend to show hyperactivity of an unproductive type, and a resistiveness to interference which appears to some extent to indicate a certain intolerance of stimuli.

Putting our experimental problem generally, we have attempted to assess the discrepancy between a subjective report of fatigue or pain experience, and a point or threshold at which the patient actually reacts physically to the experimental situation by withdrawal from it. This discrepancy region, it was fully realized by the writers, was likely to be ill-defined and unprecise, yet, until some preliminary experimenting on the problem had been carried out, it seemed impro-

bable that any more rigid controls could be devised. From clinical observation we should expect the anxiety case to have a lowered perceptual threshold for uncomfortable stimuli, and the endogenous depressive patient to have a relatively high threshold for such stimuli. We have therefore attempted to determine subjective, perceptual thresholds for both muscular fatigue and pain, as well as what have been described as reaction thresholds, in four groups of patients:

- I. Depression of the manic-depressive endogenous type.
- II. Other depressions—reactive depression, involuntional melancholia, puerperal depression, and the like.
- III. Psychoneurotics with marked anxiety producing muscular tension and sympathetic disturbance.
- IV. Other psychoneurotics, including hysterics, neurasthenics, and obsessionals.

In the present paper we shall report only results obtained for female patients.

RESPONSE TO MUSCULAR FATIGUE IN DEPRESSIVE AND NEUROTIC PATIENTS.

Guttman and Rimoldi (1941) attempted to find some answer to the problem of evaluating attitude to fatigue in various neurotic patients. Although pointing out that we do not learn from descriptions of the "fatigue" symptoms in textbooks of psychopathology whether this fatigue is objective or subjective only, they did not in fact attempt to make any threshold determinations which might throw light on this. They used the standard Mosso ergograph as a performance test in an attempt to analyse variations in the work-curve shown by their patients. They observed as typical of some of their hysterical patients a tendency to stop prematurely, while they observed an irregularity in the work-curves of the anxiety patients, which they interpreted as being due to some central interference.

Although we realized early on that the standard ergograph was likely to be unsatisfactory for any large-scale investigation, we have used this apparatus for the preliminary investigation by recording the pulls on a slow-moving kymograph. The patient was instructed to pull up on the weight, using the middle finger of the preferred hand, for as long as she could. She was told to report to the experimenter as soon as she began to feel tired. Instructions as to the nature of the fatigue feeling were not made more specific, in order to allow for the patient's own selective interpretation of what was required of her. When the patient reported feeling tired, the experimenter told her to go on until she felt she was genuinely incapable of exerting any more. In this way it was hoped to arrive at some approximate indications of the discrepancy between verbally reported perception of fatigue and a final giving up or reaction threshold. The weight used was 2 kilos, and the patient was told to try and follow the beat of a metronome set at 70 to the minute.

The results for a group of 42 female patients are shown in Table I. These patients were classified psychiatrically into the four groups already mentioned.

TABLE I.—Average Pull-number and Pull-distance (in millimetres) of the Four Groups.

		I. Endogenous depressives. (N = 5.)	II. Other depressives. (N = 15.)	III. Anxiety. (N = 10.)	IV. Other neurotics. (N = 12.)
Age :	Mean	58.2	47.3	36.8	47.4
	Range	47-76	33-66	25-54	35-69
Pull-number :					
Phase 1	Mean	142.6	260.1	48.4	51.8
	S.D.	145.1	230.0	27.0	54.8
Phase 2	Mean	14.8	66.7	165.0	76.8
	S.D.	135.0	206.2	152.4	70.7
Total 1 + 2		157.4	326.8	213.4	128.6
Percent. Phase 1 of Total.		90.6%	79.3%	27.0%	40.3%
Pull-distance (mm.) :					
Phase 1	Mean	4161	5031	806	1540
	S.D.	4064	4390	463	1664
Phase 2	Mean	186	1241	2593	1817
	S.D.	4347	6272	3399	3357
Total 1 + 2		3985	3988	2689	3036
Percent. Phase 1 of Total.		95.7%	80.2%	23.7%	45.5%

The work-curves were scored (i) by the number of pulls (= pull-number), and (ii) by the total distance pulled in millimetres (= pull-distance). Table I shows the results for two phases of the task. Phase 1 is the amount of work done up to the patient's reporting a feeling of fatigue. Phase 2 is the amount of work done after this point and up till the end of the record (the giving-up point). The percentages show the proportion of the total work-curve which occurs *before* the fatigue-feeling point, i.e., pull-number phase 1, divided by total pull-number (phase 1 + phase 2).

We shall consider mainly the pull-distance, which gives a better estimate of amount of work done than pull-number. It will be seen that groups I and II are markedly superior to III and IV in the absolute amount and proportion of work done before the fatigue-feeling point, while, after this point, the psychoneurotic groups do a greater absolute amount of work than the depressives.

As between the two depressive groups, the endogenous cases (group I) do a smaller absolute amount than group II before reporting fatigue, but a larger proportion of their total output occurs before the fatigue feeling. The anxiety cases have a lower subjective fatigue threshold than the other psychoneurotics, both absolutely and proportionally to total work done.

Although, as can be seen from the standard deviations, there is a large scatter within all groups, the following differences between mean distances pulled before the fatigue-feeling are significant by the *t* method :

For the difference between	I and III,	$t = 2.419$,	$P < .05$
" "	" II "	III, $t = 2.914$,	$P < .01$
" "	" II "	IV, $t = 2.511$,	$P < .02$

None of the other differences are significant at the 5 per cent. level.

The imperceptiveness of the depressive patients is emphasized by the number who do *not* report any feeling of fatigue before reaching a point at which they are apparently incapable of continuing the task. For such patients, "feeling tired" means "really unable to go on." In fact, 3 out of 5 in group I and 6 out of 15 in group II made no report of fatigue-feeling; whereas only 1 out of 10 in group III and 3 out of 12 in group IV had no fatigue-feeling point.

The fact that these patients made no pulls in phase 2 of the task makes the distributions of amounts done after the fatigue perception very skew, and it is thus of little value to work out the standard deviations within the groups, and the significance of the differences between their means. The trends, however, are clear, the anxiety cases doing the most work after reporting fatigue and the endogenous depressives the least.

In considering the total amount of work done, the difference between the means of groups II and III and between those of groups II and IV are not quite significant at the 5 per cent. level ($t = 1.912$ and 2.024 respectively), but the difference between all the depressives and all the psychoneurotics is significant ($t = 2.180$, $P < .05$).

It is to be noted that group I, although on the average 20 years older than group III, do an average of over five times as much work before saying they are tired, and have a slightly greater total output. It is possible that there may be a relationship between age and insensitivity to fatigue, but groups II and IV have a very different performance, although their average ages are the same, and the ranges very similar.

If the pull-number is considered, the same relationships hold as with pull-distance. Groups I and IV have a longer average pull (27.6 mm. and 26.1 mm. respectively), and groups II and III a shorter (19.2 mm. and 15.9 mm.). No explanation can at present be offered for this fact.

One further aspect of the work task which we have studied is the slope of the pull-lengths from the start of the work-curve to the finish. The curves were approximately graded as follows :

+ 2, Steep	= 1 mm. decrease in pull length in less than 15 pulls.
+ 1, Moderate	= 1 " " " " 15-25 pulls.
0, Flat	= 1 " " " or increase in over 25 pulls.
- 1, Moderate	
reversed	= 1 " increase in length in 15-25 pulls.
- 2, Steep	
reversed	= 1 " increase " less than 15 pulls.

The distribution of the 42 patients on this 5-point grading is shown in Table II.

TABLE II.—*Number of Patients in Each Group whose Work-curve Falls into Each of the Five Grades of Slope.*

Slope.	Group.			
	I.	II.	III.	IV.
+ 2	4 .	1 .	2 .	5
+ 1	1 .	2 .	2 .	1
0	—	12 .	6 .	3
- 1	—	—	—	1
- 2	—	—	—	1

Here there is a marked difference between groups I and II, all 5 patients in group I showing a considerable drop in pull-length, only 3 out of 15 in group II doing so. The endogenous depressives apparently continue till a genuine muscular fatigue point. The other depressives are younger and probably stronger, and they possibly give up eventually through sheer boredom. The psychoneurotics are variable in their slope, 2 out of group IV actually making appreciably longer pulls at the end than at the beginning.

To summarize the fatigue results, there seems to be sufficient evidence from these preliminary studies that depressive patients show considerably less sensitivity to fatigue, and have a higher subjective threshold for fatigue perception, than do the psychoneurotics. Of the subgroups of these two main categories, the endogenous depressives are the most insensitive to fatigue, and the anxiety patients the most sensitive.

PAIN PERCEPTION AND REACTION THRESHOLDS.

Since the reporting of the Hardy-Wolff-Goodell radiant-heat pain apparatus in 1940, many studies of various aspects of pain using this apparatus have been carried out in the U.S.A. In psychoneurotic patients, Chapman *et al.* (1949) found no significant difference in the average perception point when compared with a normal group. They did, however, find a significant difference in *reaction* point, the psychoneurotics tending to react either by wincing or withdrawing their heads from the stimulus earlier than the normals. This observation was confirmed by Schilling and Musser (1948), who were concerned with the possibility of using the apparatus as a test to aid in the diagnosis of neurocirculatory asthenia, effort syndrome, and anxiety neurosis. As there was quite a large *overlap* between the reaction point distributions for neurotics and non-neurotics, the authors concluded that "a normal pain reaction threshold is not evidence against the existence of psychoneurosis, since a considerable number of severe psychoneurotics showed normal pain reaction thresholds." The same authors (1949) also studied the pain reaction threshold in patients having menopausal syndrome (none being psychotic), and found that 23 per cent. of these patients showed a fusion of perception and reaction thresholds, whereas none of the normal control group showed this phenomenon.

Until much further research has been undertaken with the object of refining the experimental procedures, particularly from the psychological aspect, it is doubtful whether the test can be of more than corroborative value for this kind of case. We have, however, begun to investigate the possibility of its use on a limited group of patients, the purpose of the study being similar to that already described in the fatigue investigation. It should, it seemed, in what was clearly a difficult problem requiring long and thorough study, be a useful first step to try and assess pain perception and reaction thresholds in the endogenous depressives, and compare these with other depressives, anxiety neurotics, and other neurotics, on the hypothesis that a very similar kind of late perception to that shown in the work-task would be shown by the former.

The apparatus used is a modified version of the Hardy-Wolff, the heat from a 1000-watt bulb being focused through lenses on to an aperture in a vertical screen. A revolving disc is so constructed that the light falls on and through the aperture for 3 secs. in each minute. The patient rests his forehead against the aperture so that the light falls on an area approximately $1\frac{1}{2}$ in. above the top of the nose. He is told that he is to report the first occasion on which the heat begins to be at all painful, as opposed to warm or hot. The heat intensity is raised on a sliding resistance, beginning at a point which is only just perceptible, then rising by fixed stages

until the pain perception threshold is reached. The heat is then raised again until the patient reacts either by wincing or by withdrawing from the aperture. In the American publications the readings are taken by means of a radiometer, placed at the aperture whenever the threshold points are reached. These are expressed in gm./calories per cm.² In our own modification we have used a photo-electric cell set at the end of a tube 12 in. from the bulb. Readings are taken on a microammeter scale, and range, for this apparatus, from 60 to 320.

Results of testing 57 female patients classified as I endogenous depressions, II other depressions, III anxiety cases and IV other psychoneurotics are shown in Table III. The final column in the Table (per cent. with discrepancy) gives the percentage of cases in each group who have separate perception and reaction points.

TABLE III.—*Pain Perception and Reaction Thresholds for 57 Female Depressives and Psychoneurotics.*

Group.	N.	Age range.	Mean age.	Pain perception threshold.			Pain reaction threshold.			Per cent. with discrepancy.
				Mean.	Range.	S.D.	Mean.	Range.	S.D.	
I	4	42-62	51.0	.293	275-320	—	.299	275-320	—	25
II	26	29-60	46.6	.239	75-320	79.1	.262	150-320	52.2	42
III	15	25-54	40.5	.189	60-275	60.6	.223	110-320	60.6	60
IV	12	25-66	43.8	.225	75-320	55.3	.267	200-320	38.8	67

The statistical significance of the differences between the means for pain perception and reaction thresholds for the four groups is shown in Table IV, where values for *t* and the corresponding probability of chance occurrence (*P*) are given.

TABLE IV.—*Significance of the Differences between Means for Pain Perception and Reaction Thresholds.*

Groups compared.	Pain perception means.			Pain reaction means.		
	<i>t</i>	<i>P</i>		<i>t</i>	<i>P</i>	
I : II	1.534	> .10		1.354	> .10	
II : IV	0.608	> .10		0.289	> .10	
III : IV	1.485	> .10		2.073	< .05	
II : III	2.274	< .05		2.081	< .05	
I : IV	2.231	< .05		1.577	> .10	
I : III	3.185	< .01		2.290	< .05	

From these tables it will be seen that the endogenous depressions (group I) have higher perception and reaction thresholds than any of the other three groups, the perception difference being statistically significant as between I and III and IV but not between I and II, while reaction difference is significant only as for I and III. Of the four patients in this group, only one shows any discrepancy between perception and reaction points. The remaining three all react to the heat-stimulus by withdrawal from it, while two of them deny that it has been "what they would call painful" even at this point. While the cases in this group are too few for us to arrive at any conclusion, results do indicate a very marked imperceptiveness to painful stimulation, in comparison with the other clinical groups.

The patients of group II (other depressions) show a very much greater intra-group variability particularly in perception of pain, as is indicated by the large standard deviation (79.1). From Table IV it will be seen that II differs significantly in perception and reaction points only from group III. Inspection of individual results for this group shows that 16 out of the 26 cases have a perception point at or above 250, and 7 of these 16 perceive pain at 280 or over. In the two psychoneurotic groups only 1 out of the 27 cases has a perception point above 280. On the other hand, 8 of these depressions show an early perceptiveness to pain that is very similar to the response of our anxiety cases. This wide scatter within the group therefore would indicate that, with regard to pain tolerance, some of the depressions have an attitude towards the task of "putting up with things that are

unpleasant." Judging by their verbalizations, they are not necessarily less sensitive, in that they may perceive warmth and heat as early as many of the neurotics, but they have a central attitude which inhibits complaint of pain until they may feel the stimulus really threatens to damage them; other patients, however, of this group show no such obsessional characteristic.

With regard to the two groups of psychoneurotics (the anxiety cases, group III, and other psychoneurotics, group IV), it is notable that the anxiety cases have by far the lowest average perception threshold (189) (significantly different from both depressive groups), while their average reaction threshold (223) is slightly below the lowest perception threshold (225—group IV) of the remaining groups. They differ significantly from all the other three groups in this respect. They tend therefore both to perceive pain and to react to it earlier than the other patients. Six out of the 15 anxiety cases (40 per cent.) have no discrepancy between perception and reaction points, but this, of course, is a very different kind of fusion to that which occurs in patients of the two depressive groups. Here the fusion is due to a marked *lowering* of reaction threshold, so that the patient winces or withdraws in anticipation of the stimulus being painful. In the depressives, on the contrary, the fusion is due to a *raising* of the perceptual threshold. Not all anxiety cases, however, show this type of performance, and the level of the thresholds may be related to the severity of the anxiety symptoms.

The patients of group IV show mean perception and reaction thresholds similar to those of depressive group II, and do not differ significantly in either respect from this group. In figures, the difference between the two groups appears chiefly in the greater intra-group variability of the latter (standard deviations for perception and reaction points being 79.1 and 52.2, as compared with 55.3 and 38.8 for the psychoneurotic group), and in the fact that 8 out of 12 group IV patients (67 per cent.) have a perception point distinct from reaction point, whereas only 11 out of 26 (42 per cent.) of the group II depressives have any discrepancy between the two thresholds.

While there is much overlap in the results between the four groups of patient, and while we cannot with our present number of cases come to any definite conclusions from our findings, these observed differential trends seem worthy of a much fuller experimental investigation.

DISCUSSION.

Results from these experiments so far indicate certain quite marked differences between the groups, corresponding fairly closely with clinical hypothesis. The endogenous depressions have a very high subjective threshold for pain, sometimes suggesting a psychological indifference to the stimulation, the first and only reaction to which may be sharp withdrawal from the painful situation, with no anticipatory response whatever. The figures would also indicate that these patients may be extremely persevering in a fatigue task, and are capable of continuing without any report of subjective tiredness until apparently unable to make any further effort.

The other depressives, reactive, involuntal, and so on, are less perceptive of pain than either of the neurotic groups, but are much more perceptive than the true endogenous cases. Within this group we find quite a wide variability. On the one hand we find cases who approach the endogenous in their tolerance of pain, and on the other hand, cases who are much nearer to the anxiety patients in having a markedly low subjective threshold. They also seem to show relative insensitivity on the fatigue task, and have a higher average productivity than any other group. A few of these patients, however, show quite openly an attitude towards the task of "sticking it out," and going on as long as they can without giving up—this seems, from questioning, to represent an attitude which is quite general to their habitual way of living.

With regard to the anxiety cases, they show, as was to be expected from the previous work on heat-pain tolerance, a much lower subjective pain threshold than any other group. Not only are they hypersensitive, however; they also tend to be hyper-reactive, in that some withdraw altogether from the stimulus before it has, in fact, had time ever to hurt them. Similarly, the fatigue task shows them to be the least persevering of the groups, and to have the lowest subjective threshold for fatigue feeling, although they do not differ significantly from the other neurotics in actual total of work done.

Finally, the other neurotics, hysterics, neurasthenics, and others, do not appear markedly sensitive to pain stimulation. Here they are more akin to the depressives than to the anxiety cases, although perhaps showing considerably less variability than the former in this respect. On the fatigue task, however, they are much nearer to the anxiety patients, both in absolute amount of work done and in early complaint of tiredness.

We may conclude, therefore, that, even though these results are only preliminary, the experiments have shown certain quantitative and qualitative differences in pain and fatigue thresholds in groups of affective and psychoneurotic disorders which provide some objective confirmation for clinical hypotheses. Further development of this kind of experimental approach may give such tasks a useful place in clinical diagnosis.

A further clinical implication provided by these tasks may be found in certain cases of reactive depression which at the onset appear to be an anxiety neurosis following upon, for example, a bereavement or financial loss. It is possible that these tasks could be used initially as a guide to the outcome of the illness, and might help to indicate that a psychotic development has taken place in the course of what was originally an anxiety reaction. If this is true, and it seems to us feasible and in agreement with clinical experience, at some point in the development of severe anxiety with affective disturbance, the physiological mechanism of restoration within the body breaks down or undergoes a change. The capacity for work suffers, and the threshold to external afferent stimuli changes. The anxiety now has become a depressive psychotic reaction. This is in keeping with what we know of reactive depressive psychosis. At such a point in the illness psychotherapy becomes very much less effective, and, in contrast, shock treatments—with their profound physiological effect—may be indicated.

Many disappointments are experienced in clinical practice with just such cases, who initially appear to offer an excellent prognosis with psychotherapy, but who eventually become depressed and attempt suicide.

In the light of recent work on the adrenal cortex and endocrine function in depressive conditions and in connection with E.C.T., it seems to us likely that this alteration in an anxiety state may be correlated with an endocrine dysbalance and perhaps adrenocortical insufficiency or failure.

The authors are now engaged in experimental work directed towards this question, and it remains to be seen whether the pain and fatigue thresholds change after E.C.T. in depression and other illnesses and whether the results of adrenocortical response tests alter correspondingly. It is hoped to make this the subject of a subsequent communication.

SUMMARY.

Certain clinical aspects of pain and fatigue tolerance in depressive and psychoneurotic patients are outlined with a view to providing hypotheses for experimental investigation.

Differences in subjective feeling for and physical reaction to fatigue and pain have been investigated in female patients classified into four groups:

- I. Endogenous depression.
- II. Other depressions.
- III. Anxiety states.
- IV. Other psychoneurotics.

In the fatigue study, using an ergograph, 42 female patients were investigated. Both groups of depressives had markedly higher subjective fatigue thresholds than either of the psychoneurotic groups, the endogenous depressives and anxiety cases being at the two extremes in this respect. Both depressive groups did a greater amount of work than the psychoneurotics.

In the pain study, using a modified version of the Hardy-Wolff thermal stimulator, 57 female patients were investigated. The anxiety cases have a very low perceptual sensitivity to pain, in marked contrast to the endogenous depressives, who appear insensitive. The other depressives show considerable intra-group variability.

Clinical implications, and possible diagnostic value, of these preliminary studies are briefly discussed, together with some indications for further research.

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OBSERVATIONS ON THE RELATION BETWEEN INSULIN COMA
DOSAGE AND PROGNOSIS IN SCHIZOPHRENIA.

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THE evidence for somatological differences between various types of schizophrenia and its different stages of severity or chronicity is still scanty and often contradictory. The present investigation mainly concerns itself with endocrinological factors. Kraepelin, already, suggested disturbances in the endocrine system. The incidence of schizophrenia in different age-groups, especially its steep rise at puberty, reaching its peak at 20 in men and 25 in women and the rapid decline of its occurrence after these ages (Haas, 1938), has for a long time pointed to the sex steroids as an important factor in the pathology of this disorder. Hemp-hill *et al.* (1944, 1945, 1948) found an atrophy of the testes in many cases of schizophrenia, and considered the severity of the testicular change to be proportional to the severity of the psychosis. They suggest that the testicular lesions are not the cause of schizophrenia, but probably effects of the "pathogenic process" and related to hypothalamic or pituitary function. In confirmation of these findings Hoskins and Pincus (1949) observed the output of androgen in schizophrenics to be significantly lower than in normal men. Sears (1937) made similar observations in females, and found that the blood-œstrin level of female schizophrenics was much lower than in normal women. Possibilities for primary endocrinological factors suggest themselves; the "pathogenic process" can, however, still be primarily a psychological "stress" in this new constellation or a combination of both, or the effect of another central disturbance. Some of our somatological findings can, therefore, tentatively be interpreted as related to or identical with the primary stress or others only as secondary correlates or results, though the present state of our knowledge does not yet allow a final decision as to what is primary and what only secondary. Recent evidence on the relationship of sex hormones and insulin (Houssay, 1951) suggests that oestrogens have a "sensitizing" and androgens a "desensitizing" effect. An investigation into the insulin sensitivity in clinically different schizophrenic groups and the two sexes expressed in the amount of insulin needed to produce a hypoglycaemic coma should, therefore, throw some light on other endocrinological mechanisms.

METHOD.

In insulin coma treatment of schizophrenia, the insulin dosage is gradually increased until high enough to produce a coma within three hours after the injection, characterized by the absence of purposeful responses. The first dose producing a coma is referred to as the initial coma dose. As the dosage needed to produce comas fluctuates during the course of treatment, the maximal and minimal dose was also recorded. Treatment responses were assessed by questionnaire and/or interview. Atypical cases of schizophrenia, of the pseudoneurotic type or cases with marked manic-depressive, anxiety hysteric or obsessional features were always treated separately. The body index type was determined with the help of the Rees-Eysenck formula. The other data are self-explanatory from the tables. The weight referred to is always the one before treatment commenced. All findings were statistically evaluated.

Results :

TABLE I.—*Sex Differences.*

	Male means.	Female means.	Differences.	t.	df.	p.
Initial dosage	433·8	199·9	233·9	4·445	82	<·01
Maximal dosage	496·6	257·7	238·9	4·163	81	<·01
Minimal dosage	144·7	128·4	16·3	1·181	81	<·05

Note on degrees of freedom.—There were 14 good- and 18 poor-response males, and 36 good- and 17 poor-response females. The fluctuations in degrees of freedom arise because certain measurements were missing in the case of some females.

TABLE II.—*Light Males vs. Heavy Females.*

(Mean male weight—56·15 kgm. Mean female weight—66·15 kgm.
All females heavier than all males.)

	Light male means.	Heavy female means.	Difference.	t.	df.	p.
Initial dosage	686·7	175·0	511·7	3·011	19	<·01
Maximal dosage	771·1	240·0	531·1	2·710	18	<·02

TABLE III.—*Sex Differences in Response Grades : Schizophrenics.*

Response Grades.	1.	2.	3.	4.	5.	Totals.
Males	3	12	32	3	18	68
Females	15	21	19	6	17	78
Probability that difference in proportions is accidental	<·01	>·05	<·01	>·05	>·05	

TABLE IV.—*Sex Differences in Response Grades : Atypicals.*

Response Grades.	1.	2.	3.	4.	5.	Totals.
Males	—	—	3	1	—	4
Females	4	5	8	—	—	17
Probability that difference in proportions is accidental	>·05	>·05	>·05	>·05	—	

TABLE V.—*Differences between Female Schizophrenics and Female Atypicals of All Grades.*

	Mean schizs.	Mean atypical.	Difference of means.	t.	df.	p.
Body index	110·310	113·250	2·940	1·664	85	>0·05
Weight	56·870	53·824	3·046	1·741	92	do.
Initial dosages	208·08	178·82	29·26	1·265	93	do.
Maximal dosages	262·37	226·47	35·90	1·304	91	do.
Minimal dosages	128·09	91·88	26·21	2·701	90	<0·01

TABLE VI.—*Differences between Good-response and Poor-response Patients.*

	Good response means.	Poor response means.	Difference of means.	t.	df.	p.
Male weight	67·69	65·52	2·17	·565	30	>·05
Female weight	57·65	57·15	0·50	·277	50	do.
Male body-index	101·3	101·5	0·2	·124	30	do.
Female body-index	108·9	110·2	1·3	·578	47	do.
Male initial dosage	380·0	475·6	95·6	·715	30	do.
Female initial dosage	191·2	218·2	27·0	1·224	51	do.
Male maximal dosage	452·9	541·7	88·8	·602	30	do.
Female maximal dosage	243·6	289·4	45·8	1·682	50	do.
Male minimal dosage	156·4	135·6	20·8	·780	30	do.
Female minimal dosage	121·1	144·7	23·6	1·574	50	do.

TABLE VII.—*Comparison between Male and Female Schizophrenic Patients, Grades 1 and 2.*

	Male mean.	Female mean.	Difference of means.	<i>t.</i>	<i>df.</i>	<i>p.</i>
(a) <i>Under 6 months :</i>						
Initial dosage	476.67	185	291.67	4.327	26	<0.01
Maximal dosage	558.33	243.182	315.148	4.358	26	do.
Minimal dosage	171.67	119.54	52.13	2.531	26	<0.05, >0.01
(b) <i>Over 1 year :</i>						
Initial dosage	356.67	160	196.67	2.220	7	>0.05
Maximal dosage	428.33	226.67	201.66	2.175	7	do.
Minimal dosage	171.67	100	71.67	1.234	7	do.

TABLE VIII.—*Comparison between Male and Female Schizophrenic Patients, Grade 3.*

	Male mean.	Female mean.	Difference of means.	<i>t.</i>	<i>df.</i>	<i>p.</i>
(a) <i>Under 6 months :</i>						
Initial dosage	278.57	210	68.57	1.013	10	>0.05
Maximal dosage	308.57	252	56.57	.944	10	do.
Minimal dosage	121.43	140	18.57	.535	10	do.
(b) <i>Over 1 year :</i>						
Initial dosage	352	265	87	1.134	21	>0.05
Maximal dosage	458	328.76	129.24	.972	21	do.
Minimal dosage	148	146.25	1.75	.064	21	do.

TABLE IX.—*Comparison between Male and Female Schizophrenic Patients, Grades 4 and 5.*

	Male mean.	Female mean.	Difference of means.	<i>t.</i>	<i>df.</i>	<i>p.</i>
(a) <i>Under 6 months :</i>						
Initial dosage	260	198.57	61.43	.729	10	>0.05
Maximal dosage	274	232.86	41.14	.528	10	do.
Minimal dosage	94	138.57	44.57	1.284	10	do.
(b) <i>Over 1 year :</i>						
Initial dosage	540	206.25	333.75	1.888	20	>0.05
Maximal dosage	620.714	273.75	346.96	1.769	20	do.
Minimal dosage	143.57	126.25	17.32	.585	20	do.

TABLE X.—*Comparison between Male Grades 1 and 2 (short duration of illness) and Male Grades 4 and 5 (long duration of illness).*

	Under 6 months. Grades 1 and 2 mean.	Over 1 year. Grade 4 and 5 mean.	Difference of means.	<i>t.</i>	<i>df.</i>	<i>p.</i>
Initial dosage	476.67	540.0	63.33	.287	18	>.05
Maximal dosage	558.33	620.71	62.38	.258	18	do.
Minimal dosage	171.67	143.57	28.10	.831	18	do.

TABLE XI.—*Comparison between Female Grades 1 and 2 (short duration of illness) and Female Grades 4 and 5 (long duration of illness).*

	Under 6 months. Grades 1 and 2 mean.	Over 1 year. Grade 4 and 5.	Difference of mean.	<i>t.</i>	<i>df.</i>	<i>p.</i>
Initial dosage	185.0	206.25	21.25	1.042	28	>.05
Maximal dosage	243.18	273.75	30.57	.994	28	do.
Minimal dosage	119.54	126.25	6.71	.367	28	do.

TABLE XII.—*Body Index Figures.*

	Mean I.B.	S.D.I.B.	N.
Rees-Eysenck normals . . .	100.10	5.82	100
„ „ neurotics . . .	102.44	6.97	400
Netherne schizophrenics . . .	101.39	6.34	68

VERBAL INTERPRETATION OF TABLES.

Table I.—The mean initial and maximal doses for males are higher than those for females to a degree that is most significant statistically. The sex difference in minimal dosage is not statistically significant, though the mean for females remains lower.

Table II.—The males, as a group, are significantly heavier than the females, but the sex difference in initial and maximal dosages cannot be attributed to this difference in mean weight. If the twelve females above the midpoint between male and female mean weights are contrasted with the nine males below the midpoint, two groups result in which all females are heavier than all males and in which the female mean weight approximates the total male mean, the male mean weight to the total female mean. The male initial and maximal dosages remain higher than the female to a statistically significant extent.

Table III.—Shows differences in treatment response grades between male and female schizophrenics.

- Grade 1 = Total recovery.
- Grade 2 = Social recovery.
- Grade 3 = Social defect.
- Grade 4 = Family invalid.
- Grade 5 = Hospital invalid.

The response grades correspond to the classification of Guttman, Mayer-Gross and Slater (1939) :

Total recovery = Freedom from symptoms and signs, return to previous social environment and to previous or equivalent occupation.

Social recovery = Return to previous social environment and to previous or equivalent occupation, in spite of the presence of minor signs and symptoms, such as irritability, shyness, shallowness of affective response, etc.

Social defect = Presence of minor symptoms, as over, incapacity to carry out work of previous level, and failure to maintain self in the same degree of social adaptation.

Family invalid = Presence of well-marked symptoms, incapacity to carry out any useful occupation, but manageable at home.

Hospital invalids = The inmates of mental hospitals, some continuously since the end of treatment, some relapsed after a temporary recovery.

The proportion of female schizophrenics giving therapeutic response 1 is significantly greater than the proportion of male schizophrenics doing so. The proportion of females giving response 3 is significantly less than the proportion of males. There are no significant differences between the sexes in the proportions giving responses 2, 4 and 5.

Table IV.—This indicates that among atypicals there are no significant differences between the sexes in the proportions giving the various therapeutic responses. The comment with regard to the small number of males is again relevant. The proportion of females giving responses 1 and 2 is definitely greater than the proportion of males. Amongst all atypicals of both sexes only one patient showed response 4, and none response 5.

Table V.—This indicates that there are no significant differences between schizophrenic and atypical females in regard to body-index, weight, initial or maximal dosage, though the schizophrenics show significantly higher minimal dosages. All atypical dosage means are lower.

Table VI.—If all atypicals are excluded, no statistically significant differences within each sex are seen between good (response grades 1 and 2) and bad (response grades 3 and 4) response patients as regards weight, body-index and insulin dosage, though insulin coma dosage means are higher in the poor-response cases except for the male minimal dosage.

Table VII.—Once response 1 and 2 cases are classified according to duration of illness, it becomes evident that the initial, maximal and minimal dosage in patients with a duration of illness of less than six months is significantly lower in females than in males. This difference is not seen once if the duration of illness is more than one year.

Tables VIII and IX.—Treatment responses 3, 4 and 5 show no significant difference in dosage whether the duration of illness is long or short.

Tables X and XI.—A comparison between response grades 1 and 2 with a duration of illness of less than six months, and response grades 4 and 5 with a duration of illness of over one year, reveals no statistically significant differences within each sex, though there is a trend for the dosage means to be higher in the group having a poor response and long duration of illness.

Table XII.—The Netherne schizophrenics do not differ significantly either in mean or in standard deviation from the Rees-Eysenck normals, nor from the Rees-Eysenck neurotics.

SUMMARY OF CHIEF FINDINGS.

(1) *Sex and Dosage.*

The mean initial and maximal dosages for males are significantly higher than those for females, whatever the therapeutic effect, and this is independent of weight.

(2) *Sex and Therapeutic Effect.*

(a) Significantly more females than males make a total recovery. (Response grade 1.)

(b) Significantly more males than females exhibit the response—social defect. (Response grade 3.)

(c) There are no significant differences between the sexes in the numbers of social recoveries, family invalids and hospital invalids. (Response grades 2, 4 and 5.)

(3) *Sex, Dosage, Therapeutic Effect and Duration of Illness.*

(a) Females showing the therapeutic responses 1 and 2 have a significantly lower initial, maximal and minimal insulin coma dosage than males, as long as duration of illness is less than six months.

(b) Males and females show no significant differences in mean initial, maximal and minimal dosages between any therapeutic effects, if the duration of illness is over one year.

(4) *Dosage: Schizophrenics versus Atypicals or "Pseudoschizophrenics."*

(a) Atypicals or "pseudoschizophrenics" generally show better treatment responses than do schizophrenics. No response grade 5 occurs amongst atypicals and only one response grade 4.

(b) Female schizophrenics show a significantly higher mean minimal dosage than female atypicals, whose dosage means for initial and maximal doses also remain lower, though not to a statistically significant degree.

Tentative Analysis.

Let there be a factor " x " which brings about lower initial maximal or minimal coma dosages, and a factor " y " which brings about a good therapeutic response. Then findings 3(a) and 4(a) and (c) suggest strongly but do not conclusively prove that " x " and " y " are either identical or closely dependent on each other.

Findings 2(c) and 3(b) can be accounted for by postulating a factor " z " in whose presence the therapeutic value of " $y = x$ " is nullified. If factor " $x = y$ " is identified with endocrine events, factor " z " might plausibly be identified with chronicity, expressed in duration of illness, or severity of illness—(findings 3(a) and (b)). Finding 4 suggests that factor " $x = y$ " is more strongly operative in atypicals than in schizophrenics. This factor appears more strongly linked with female sex (findings 1, 2(a) and (c)).

DISCUSSION.

General Endocrinological Considerations.

In considering endocrine mechanisms it is important to attempt a dynamic evaluation of the situation. The different hormones of the anterior pituitary, usually referred to as trophic, stimulate their respective target glands, and hypersecretion of the trophic hormone leads to hypersecretion and hyperplasia of the target gland. After prolonged stimulation the target gland may become refractory to stimulation. Target gland hormones inhibit the production of their corresponding trophic hormones. The responses of body-cells vary considerably to the different hormones, and are dependent on innate genetically determined factors as well as environmental ones (Williams, 1950). The sensitivity of the endorgan is of great importance in assessing the quantitative and qualitative effect of a hormone. The mechanism of release is another important factor, and whether this is inhibited or sensitized. Some authors (Sackler *et al.*, 1951), therefore, also talk of an operational activity of a particular hormone determined by all these factors, and the inhibiting or activating influences of different hormones on each other.

The different mechanisms determining the sensitivity to insulin were reviewed by several authors (Martin, Martin, Lyser and Strouse, 1941; Smeto, 1948; Axelrod, Lobe, Orton and Meyers, 1947). Anterior pituitary extracts are known to be antagonistic to insulin (Williams, 1950). This is probably effected by more than one pituitary hormone (Young, 1944). Marked resistance to insulin develops during treatment with such extracts. This effect does not occur in adrenalectomized animals. Hypophysectomy leads to insulin hypersensitivity (Houssay and Biasotti, 1941). Patients suffering from Addison's disease are known to be extremely sensitive to insulin. Recent evidence suggests, however, that the action of insulin is antagonized both directly by the pituitary and indirectly through the adrenal cortex (Williams, 1950). Oestrogens also influence anterior pituitary function. Clinically and experimentally they were found to stimulate initially and later to depress. If given in large doses over a prolonged period the ovaries may eventually become inactive (Everett, 1950). There is also some evidence that oestrogens depress the release or effectiveness of the diabetogenic principle (Williams, 1950). This might explain why diabetes is much more common in males than in females and, further, why the incidence in females rises in later decades. It is, for instance, found that menopausal diabetes responds favourably to oestrogen therapy (Thorn and Forsham, 1950). An increase in insulin requirements occurs if testosterone is given to diabetics (Thorn and Forsham, 1950). The incidence of diabetes in partially depancreatized rats is also diminished by oestrogens and increased by androgens. Oestrogens and androgens appear to be antagonistic in this respect (Houssay, 1951). The pituitary can, however, be inhibited by testosterone also, though it is less sensitive to it than to oestrogen. Large doses of testosterone were found to lead to a reduction of the sperm count presumably by a depression of gonadotrophin output (Engle, 1942). As mentioned above, there is evidence to show that this antagonism does not affect the "diabetogenic principle."

Results of General Endocrinological Interest.

Houssay (1951) concludes that "substances with oestrogenic effect decreased the incidence of diabetes . . . following subtotal pancreatectomy, androgens on the contrary increased it." Sex differences in insulin coma dosage are probably explained by similar mechanisms. Excessive adrenal hormone can also be the cause of diabetes (Cushing syndrome, Archard Thiers syndrome and adrenal tumour). The insulin resistance seen in many diabetics can be due to an increased output of the anterior pituitary or the adrenal cortex. The necessity for large insulin coma dosage can at times be explained in this manner. High initial and maximal insulin coma dosages may be required because of a strongly effective suprarenal cortical hormone. Little fluctuation in the coma dosage may indicate a strong reserve power, and low minimal dosages signs of refractoriness or exhaustion.

If the effects of high insulin dosage used in insulin coma treatment are looked upon as a special instance of a "stress response," then the fluctuations and differences in response can also be interpreted in terms of the "general adaptation

syndrome." This syndrome according to Seyle (1950) has three stages, the alarm stage, the stage of resistance and the stage of exhaustion. High doses are then an instance of a highly effective alarm stage characterized by a discharge from a strong adrenocortical reserve and very low doses one of exhaustion.

In the present investigation an attempt is made to explain the change in insulin sensitivity on an endocrinological basis; this is probably a simplification.

Results with Reference to Endocrinological Mechanisms in Schizophrenia.

It need hardly be said that our findings cannot be claimed as definitely specific for schizophrenia as other diagnostic categories were not examined; some can only be tentatively assumed as acting in a more specific manner. It is also possible that the type of clinical syndrome may depend on other physiological characteristics of the tissues especially affecting central nervous system function. These are probably determined by constitutional factors, which again result from an interplay between genetic and environmental influences. If the latter conception is true, it also follows that different pathological endocrine processes may result in similar psychological syndromes, or that different psychological syndromes may be related to the same endocrine pathology. This hypothesis appears the most likely explanation of the evidence collected by various workers in this field.

Meduna (1950) states that the schizophrenias responding favourably to shock therapy are better classified as pseudoschizophrenias, because of special clinical characteristics such as similarities with the oneiroid state of Mayer-Gross or other atypical features referred to above. Refractory cases are, according to Meduna, suffering from an "endogenous schizophrenia." Meduna believes that prognostically favourable groups also have certain endocrinological features, e.g.,

- (1) A sustained blood-sugar curve in the intravenous glucose tolerance curve.
- (2) A positive diabetic-like blood-sugar curve in the Exton-rose test.
- (3) Resistance to insulin in the intravenous insulin-tolerance test.
- (4) An increased anti-insulin factor in the blood.

He suggests that all this may be explained by an overactivity of the anterior pituitary. Other authors (Hoskins, 1946) state that differences in glucose tolerance curves are consistently related only to different degrees of emotional tension. Cases with marked tension showed the most sustained curves. These conditions are more predominant in prognostically favourable cases and, therefore, need not be explained by an "anti-insulin factor." If Meduna's interpretations were correct, a need for larger doses of insulin to produce comas in prognostically favourable cases should be revealed. Our findings do, however, show the opposite. Atypical cases (symptomatic or pseudoschizophrenias) have lower coma dosage means than typical schizophrenias. They also show the best response grades. The fact that the minimal doses are significantly lower in atypical cases may indicate that true schizophrenias with a comparatively short duration of illness have a greater operational effectiveness of suprarenal pituitary function. Tsai, Bennett, May and Gregory (1950) found eosinopenia as an indication of a release of suprarenal cortical hormone during insulin coma treatment. Is then a favourable response to treatment associated with a decrease of cortical hormone activity from an abnormally high down to a lower normal level? The release of the hormone during hypoglycaemia may also be related to the reactivation of the psychosis often seen at the beginning of treatment.

Our finding that there is a greater number of good responses amongst female patients than amongst males and at the same time that the latter generally require higher dosages does point to the sex steroids as an important factor in this mechanism. Is the more potent inhibitory effect of the oestrogen on the anterior pituitary related to better prognosis? Is one justified in assuming an initial overactivity of the pituitary, possibly explained by the experimental findings showing an initially stimulating effect of oestrogen on pituitary function, as an aetiological factor for the development of the psychosis? Sackler, A. M., *et al.* (1950) came to similar conclusions. In favour of this hypothesis they quote the observation that A.C.T.H. or cortisone have led to psychotic reactions. They also found that sex steroids raised eosinophil levels, the greatest increase occurring in those patients attaining improvement. As adrenocortical hormones are known to lower the eosinophil level, sex hormones are believed to have in this respect an anti-adreno-

cortical effect. Similar observations (Sackler *et al.*, 1950) are reported with lymphocyte/neutrophile ratios which became higher following steroid therapy in favourably responding cases. An increased adrenal cortical activity occurs during insulin coma treatment, electroconvulsion therapy and electronarcosis (Ashby, 1949; Mitchelson and Hutchins, 1948; Parsons *et al.*, 1949; Rees, 1949). As mentioned before, experimental findings show that oestrogens initially have a stimulating effect on the anterior pituitary. This might occur with the onset of puberty when the organism is flooded with sex steroids, and if the response to this stress is abnormal it might also serve as an explanation for the rise in incidence of schizophrenia at this period of life. Previous studies on the sex incidence of schizophrenia are of great interest in this connection. Haas (1935) found that amongst a total of 15,433 male and 10,228 female admissions during 1924-1933 the diagnosis of schizophrenia could be made in 13.3 per cent. of the males and in 28.03 per cent. of the females, or 100 male first admissions corresponded to 123.2 female ones. The conclusion was therefore reached that the incidence of schizophrenia was higher in females than in males. The sex difference amongst first admissions does vary in the different age-groups. Haas (1938) found that in the age-groups of 16-20 females were more frequent than males. In the age-group of 20-25 the figure for males was found higher, and during the involutional period it is again the females who are greater in number. Dayton (1940) and Malzberg (1940, 1943) made a similar investigation, but calculated these figures per 100,000 population. Their results can, therefore, be taken as more reliable. They also found a higher incidence for females during the involutional period, but in contrast to Haas a greater number of males in the age-group from 10-39. The period during which oestrogens have their maximum activity, therefore, seems to have a certain protective influence, possibly by inhibiting anterior pituitary activity. M. Bleuler's (1950) observations of acromegaloid signs in schizophrenia also point in this direction. He found the incidence of schizophrenia in acromegaloid subjects three times greater than in other members of the investigated families. The opposite was found in Simmond's disease. An acute schizophrenic psychosis may in other words be related to a hyperactivity of the pituitary with its resultant effects on target glands. All this appears contradictory to Hoagland and Pincus's (1949) views that a deficient suprarenal function is either causative or somehow related to the pathogenesis of schizophrenia. How can this discrepancy be explained? It has been found that recent cases of schizophrenia do not show this deficiency (Reiss, 1950) with nearly the same frequency. L. Rees (1951) used desoxycortone acetate and ascorbic acid in schizophrenia without effect. Contrary to Hoagland and Pincus, the response to A.C.T.H. was found positive in over 70 per cent. of all cases. Hoagland and Pincus's findings might, therefore, apply to a later stage of the disease, following overstimulation in the initial stages. The target glands might then have become refractory or exhausted, or the sensitivity of the endorgans or tissues in general altered in the course of the disease process. The 14 patients investigated all had a comparatively short duration of illness; only rarely were any with more than one year's duration of illness given insulin coma treatment.

Most workers believe that a specific organic pathology underlying each psychopathologic syndrome is unlikely (Bleuler 1951). Differences in psychopathological syndromes are rather explained by constitutional factors or different sensitivities to the organic disturbance. The evidence in support of pituitary hyperactivity and its effects in the pathology of schizophrenia is so far only suggestive and further research is required to confirm it.

SUMMARY.

(1) Lower insulin coma dosages have a tendency to be correlated with a good therapeutic response.

(2) Female schizophrenics of less than six months duration of illness needed lower dosages than males of the same duration of illness. This difference disappears with a longer duration of illness.

(3) Female schizophrenics in our series showed a better prognosis than males.

(4) Atypical cases had the lowest minimal dosages and the best therapeutic response.

(5) The body-index type was not significantly correlated with prognosis, neither was weight.

(6) The chief findings are tentatively discussed.

(7) Our findings suggest the therapeutic use of sex steroids possibly in combination with insulin coma treatment.

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THE EFFECTS OF E.C.T. ON THE DRAWINGS OF DEPRESSED PATIENTS.

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INTRODUCTION.

A STUDY of the effects of E.C.T. on mental efficiency and retentivity has already been published (Hetherington, 1952). The present paper reports the effects of E.C.T. on drawings made by the same group of patients. Workers such as Prinzhorn (1922), Maclay, Guttman and Mayer-Gross (1938), Anastasi and Foley (1943), Martin and Weir (1951) and Raven (1951) have been concerned with analysing unrestricted or "free" drawings of widely varying nature. Other workers, such as Burt (1921) and Goodenough (1926) have used restricted drawings usually of "a man" more specifically for the estimation of intelligence. Anastasi and Foley (1941) have reviewed the work done with the drawings of abnormal people, and have drawn attention to the lack of control groups, the rarity of quantitative assessments, and the danger of over-interpretation of the drawings on the part of observers. In order to meet these criticisms, patients' drawings have been compared in the present paper with those of a group of normal untreated people, assessments of the drawings being limited to quantitative measurements of area and position on the page, or to subjective judgments of consistency of style undertaken by several observers working independently.

METHOD.

Production of Drawings.

Details about the patients and controls tested in this investigation are given in the paper already referred to (Hetherington, 1952). It is only necessary to say here that the drawings were produced by 10 depressed patients undergoing E.C.T. and by a control group of 10 nurses. These 20 subjects each drew a human figure of the same sex as themselves. Each was given a standard set of coloured chalks and a standard sheet of paper, pencil and rubber. Care was taken to explain to every subject that the test was not of their drawing ability, but of the change in this ability from week to week. Although many complained that they could not draw, they were satisfied that this did not matter for the purposes of the test. All 20 subjects repeated the test three times, each producing four drawings in all. The control drawings were produced at intervals of one week, and the patients' drawings were produced at test sessions given the day before the first treatment, the day after the fourth treatment, two or three days after the final treatment, and ten days to a fortnight later.

Assessment of Drawings.

Position on page.—Drawings were assessed with respect to their position on the page. Two independent observers marked a point on each drawing which they regarded as its "centre of gravity"; and it was found that in no case were their independent assessments more than 0.3 in. apart. The mid-point of the line joining these two points was taken to be the centre of the drawing, and the distances of this point from the horizontal and vertical median lines of the page were measured in each case.* Drawings towards the left of the vertical median line were given positive measurements; those towards the right, negative. Similarly, drawings above the horizontal median line received positive measurements; those below,

* The centre of gravity could, of course, have been plotted mathematically by treating the figure as an irregular lamina; but since the figure was conceived and viewed in three dimensions, it was thought better to adopt the method indicated.

negative. The patients and controls were compared by calculating the mean distances of the centres of their drawings from the median lines of the page at each session.

Area of drawing.—Each drawing was also assessed with respect to the percentage of the page covered by it. This was done by means of a transparent grid ruled off in inch squares superimposed over each drawing, the measurement being taken to the nearest 0.5 sq. in. The patients and controls were compared by calculating the mean percentage of the page covered by each group at each session.

Consistency of style.—In order to assess the consistency of each single artist's drawings over the four sessions, use was made of 20 independent observers. All distinguishing marks were obliterated from each drawing, which was then numbered. Each observer was then asked to sort the 80 drawings according to the following instructions:

"These drawings have been made by 20 different people who have contributed four each. All you have to do is to sort them into sets, each of which you consider consists of drawings done by a single artist. It will help to tell you that all the male artists drew men and all the female artists, women. If you cannot collect four of any one artist collect as many as you can, but no set must contain more than four drawings. Any odd ones left over must be piled separately."

It was assumed that if a single artist's drawings were consistent in style over the four sessions, an observer would have no difficulty in matching them. If, however, E.C.T. were affecting an artist's drawings, it would be more difficult to do so.

RESULTS.

Position of Drawing on Page.

Table I indicates the mean distances of the centre of gravity of the drawings from the horizontal and vertical median lines of the page. It will be seen that

TABLE I.—*Position of Drawing on Page.*

Mean distances of centre of drawings from vertical (V)† and horizontal (H)ϕ median lines of the page (in inches) for each Group at each Session.

			Session I.	Session II.	Session III.	Session IV.
Controls		{ V .	+0.58	+0.36	+0.45	+0.48
		{ H .	+0.39	+0.28	+0.52	+0.07
Patients		{ V .	+1.69	+1.16	+1.02	+0.99
		{ H .	+1.29	+0.93	+0.80	+1.19
Critical Ratios	{ Between Groups	{ V .	3.02*	2.21	1.76	1.90
		{ H .	1.98	1.49	0.66	2.41
	{ Between Sessions			I + II.	II + III.	III + IV.
		{ V } { H } { V } { H }	Controls	{ 1.14 .	0.52	0.17
			Patients	{ 0.49 .	0.68	1.26
			{ 1.11 .	0.31	0.08	
			{ 0.65 .	0.26	0.75	

† Positive: to the left; negative: to the right.

ϕ Positive: above; negative: below.

* $P < 0.01$

there is one difference between the groups large enough to be considered significant by statisticians, which indicated that the patients' drawings were nearer the left-hand side of the page than the controls in Session I. The mean position of the patients' drawings was always nearer the left-hand side of the page and nearer the top of the paper in every Session than the mean position of the group of controls' drawings. Where there was a marked change of position of an individual patient's drawing on the page over the four Sessions, it was always to bring it down from the top left-hand corner to the middle of the page. No such change occurred in any series of drawings produced by the control group.

Area of the Page Covered by Drawing.

Table II shows the mean percentage area of the page covered by the drawings of the two groups. Those of the control group were surprisingly constant over the

TABLE II.—*Area of Drawings.*

Mean percentage of the page covered by drawings of each Group at each Session.

		Session I.	Session II.	Session III.	Session IV.
Controls		12.20	12.50	11.40	13.20
Patients		9.50	19.40	20.00	13.70
Critical Ratios	{ Between Groups	0.89	1.56	2.01	0.12
	{ Between Sessions	{ Controls I + II. II + III. III + IV. Patients 2.66* 0.13 1.45			

* $P < 0.02$.

sessions, while there was an increase in mean area covered by the patients' drawings between Sessions I and II which could only have happened by chance less than twice in every hundred times. The patients' drawings before treatment were smaller than those of the control group, and those made during and after treatment were larger than those of the controls.

Consistency of Style of Each Series of Drawings.

A series of drawings was taken to be consistent if at least 15 of the 20 observers correctly sorted them into a complete group of four drawings. With this criterion, 7 out of 10 of the control group and only 2 out of the patients' group were rated as consistent. The number of observers out of the 20 who successfully matched all four drawings in the case of each patient and each control is set out in Table III. The differences between the mean of the two groups was sufficiently great to be considered outside the possibility of a chance occurrence.

TABLE III.—*Consistency of Style.*

Number of observers who correctly matched all 4 Drawings in the case of each member of the two Groups of 10 artists.

	No. of artist.										Mean.
	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	
Controls	20	19	18	17	16	16	15	12	9	4	14.6
Patients	17	15	12	10	8	7	6	4	1	0	8.0

Critical ratio, 2.79*

* $P < 0.02$.

Numbers in bold type are taken to be indicative of consistency in the series of drawings.

COMMENTS AND CONCLUSIONS.

There is evidence, supported statistically, that depressed patients tend to place their drawings more over to the left of the page than normal people, and that the effect of E.C.T. is to bring the drawings over to the middle of the page. Reitman (1939), reporting on the drawings of four depressed patients, states that they tended to squeeze their drawings into the corner of the page. In our series of drawings four of the ten patients before treatment squeezed their drawings into the top left-hand corner of the page, and two produced drawings markedly displaced in the same direction. In the middle of treatment two of the ten patients squeezed their drawings into the top left-hand corner and two others displaced their drawings markedly in the same direction. A fortnight after the end of the treatment only one patient out of ten squeezed her drawing into the top left-hand corner, and only one other was markedly displaced in the same direction. There was no tendency for the drawings to be displaced in any other direction and there was no evidence of any displacement in any of the 40 drawings produced by the 10 controls.

There is also evidence, again supported statistically, that there was an increase in the area of patients' drawings after the beginning of E.C.T., whereas the series of control drawings showed no change in area. Stainbrook and Löwenbach (1944), reporting on the early post-convulsive writing of patients undergoing convulsive therapy, state that such writing is more expansive and space-filling than normal. It is therefore of some interest to note that E.C.T. produces a similar effect on the drawings of such patients even when such drawings are not immediately post-

convulsive. Schube and Cowell (1939) report excessive restraint in the drawings of depressed patients, and Liss (1938) suggests that size of drawing might give a clue to ego evaluation. Both these suggestions are well supported by our results, if we assume that decrease in size of drawings indicates at least restraint, if not ego under-evaluation.

Pfister (1934), reporting on the drawings of 431 patients of all types, says that depressed cases tended to produce monochrome drawings, often in blue or green. However, the fact that he did not provide his patients with pencils will have forced some to use a crayon instead, where otherwise they would have used pencil only. In these cases it is to be expected that they would not change the crayon for another, but would use it as a pencil, producing a monochrome drawing as a result. Our patients were provided with a pencil as well as crayons, and at each session five or six out of the ten used a pencil only, while only one or two confined themselves to a single crayon.

A change in style in the series of drawings was noticed more often in patients undergoing treatment than with normal controls, and this difference was large enough to be considered significant by statisticians. Anastasi and Foley (1942), in a research involving 680 subjects, half psychotic and half normal, state that the majority of psychotic drawings were not clearly differentiable from those of the control group, although statistically reliable differences were found in a number of specific categories. Our results suggest that when people's drawings are compared, not with those of others, but with their own, clear changes become evident during treatment.

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SUMMARY.

Ten patients undergoing E.C.T. were asked to do a drawing of a human figure before, during and after treatment. Their drawings were compared with those produced at similar intervals by 10 normal untreated people. While there was no change in the series of drawings produced by normal people, drawings produced by patients during a course of E.C.T. usually became larger, moved from the left to the middle of the page, and changed noticeably in style.

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EXPERIMENTS ON THE PROLONGATION OF INDUCED EPILEPTIFORM CONVULSIONS IN THE CAT.

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THE present paper offers a brief summary of work which has been published in German journals dealing with the prolongation of induced convulsions. In the course of my experimental research the following phenomena were demonstrated:

(1) Continuous convulsions lasting up to one and a half hours were produced by the administration of oxygen and adrenaline, preceded by the injection of phenyl-methyl-aminopropane.

(2) Prolonged convulsions of 33 minutes were produced by the intravenous injection of 2 ml. of a 10 per cent. metrazol solution and continuous oxygen insufflation.

(3) Isolated continuous convulsive activity of the cerebellum was produced lasting 30 minutes after cessation of respiration and of all cortical electrical activity. This was achieved by continuous insufflation of oxygen together with the injection of adrenaline and strychnine.

(4) Activation of a prolonged convulsion up to 11 minutes, without further electric stimulation, was effected via the thalamus by the injection of adrenaline after administration of phenyl-methyl-aminopropane and continuous oxygen insufflation.

My work was based on the following considerations: During the epileptiform fit a great increase in cerebral metabolism takes place which amounts to 20 to 50 times the normal activity if the electrical potential is taken as a yardstick (Jung, 1940). This increased metabolism uses up a correspondingly large amount of oxygen. At the same time laryngospasm may close the larynx during the fit, with resultant cessation of breathing for a short time and the onset of cyanosis. This well-known course of events suggested to me that the epileptic fit probably terminated from lack of oxygen and, perhaps, from lack of other substances needed as fuel. I furthermore concluded that a continuous supply of oxygen and an adequate blood supply to the brain might effect a prolongation of convulsions.

Experimental investigations have supported this working hypothesis. The results are based on observations on 51 cats, in whom 1,096 convulsions were induced electrically and 25 by metrazol. By the insertion of bipolar electrodes into different parts of the brain, viz., cortex, thalamus, caudate nucleus, cornu ammonis, medulla, cerebellum and spinal cord, the electrical potentials were registered by using a method modified from Hess by R. Jung (1940). Potentials from four different regions could be recorded simultaneously, and in some experiments the blood-pressure taken from the carotid arteries was noted at the same time.

Under normal conditions the convulsion induced by electricity or metrazol lasts about one minute. By insufflation of oxygen the convulsion could be extended to about three minutes. Without extra oxygen, but after tracheotomy and the administration of 0.1 mgm. adrenaline every 3-4 minutes, prolongation up to 13 minutes was possible. Under these conditions the animal resumed respiration spontaneously one minute after the beginning of the fit.

In exhausted animals with poor circulation it was possible to provoke a new, strong and prolonged tonic-clonic discharge by insufflation of oxygen alone when the convulsion had almost died down.

Oxygen prolongs the tonic phase of the convulsion, which is the phase of the most powerful discharge. With inhalation of oxygen the period of complete electrical silence observed after the "normal" fit does not take place, the convulsive pattern being directly followed by the ordinary electrical activity without interruption.

Probably other metabolites accumulated during the prolonged fit have to be removed and replaced by fresh substances before the convulsive activity can be continued further.

If the initial stimulation was *general*, as in the usual E.C.T. machines, it was observed that after 20–30 minutes of prolonged convulsions the focus of convulsive activity alternated. The focus was found to change from one hemisphere to the other, staying 1–3 minutes in each. If, however, *localized* stimulation was used to produce a convulsion, the spread of electric activity from the focus could be observed. First the convulsive pattern spread over other parts of the same hemisphere, and then after three minutes the other hemisphere, hitherto inactive, took over the excitation starting from subcortical regions, while simultaneously the hemisphere which was excited first became quiet.

This wandering of the focus from one hemisphere to the other seems essential for the prolongation of the convulsion. It appears to give the resting hemisphere time for recovery.

Metrazol, on the other hand, acts directly and simultaneously on all parts of the cortex. Hence no wandering focus can be observed if the convulsion is provoked by metrazol. Instead, periods of maximum discharge are followed by periods of rest when the convulsion is prolonged by the methods described above. There is no preference of metrazol for any single region of the brain with the exception of the cerebellum (*vide infra*).

Another observation of particular interest is the cessation of muscular phenomena and movements about three minutes after the beginning of the prolonged convulsion. The muscles are completely relaxed and remain so while the brain still shows the electric phenomena typical of the convulsion. One has to presume that blocking has taken place at some synapses between brain and muscles.

Another unexplained phenomenon is the following: if adrenaline is given during the later stages of a prolonged convulsion, the electrical activity in the cortex is increased each time without further rise in blood-pressure. A direct effect of adrenaline on the nerve cell can be suspected.

Prolonged convulsive activity of the cerebellum.—Use was made of the animal preparation with its automaton-like prolonged convulsive state to measure the survival time of different parts of the brain by noting the duration of convulsive activity. After cutting the brain stem at the level of the mammillary bodies, followed by decapitation, and complete exhaustion of the animal through repeated convulsions, it is impossible by electric stimulation to produce a seizure with tonic-clonic features. After injection of metrazol and strychnine into such an animal only small differences of potential or single bursts of convulsive activity can be elicited from the cortex; on the other hand, in this condition the cerebellum can still show persistent convulsive activity for 30–50 minutes after cessation of cortical activity, if oxygen is given continuously and adrenaline injected at the same time. Even after muscular rigidity, similar to lethal rigidity, has appeared, the cerebellar activity may continue for 30 minutes. This capacity of survival of the cerebellum has not hitherto been suspected. It may be explained by the special structure of the organ and its mode of blood supply, which being by the vertebral arteries differs from that of the cortical hemispheres.

Re-activation of convulsions by adrenaline via the thalamus.—Substances which occur naturally in the body and favour the production of convulsions are of special interest in the problem of epilepsy. As I suspected that adrenaline might be one of these substances, I designed the following experiment:

It seemed improbable that the injection of adrenaline by itself would cause convulsions, and in fact I found that even large amounts of adrenaline (several milligrammes given intravenously to cats) did not provoke fits. It is known that adrenaline is rapidly destroyed in the presence of an amino-oxydase. I therefore started the experiment by giving phenyl-methyl-aminopropane which, according to Heim, inhibits amino-oxydase and so allows a higher adrenaline level in the blood. After phenyl-methyl-aminopropane the injected adrenaline was found to be only slowly destroyed.

The next step was to induce a convulsion in the experimental animal by electric stimulation and prolong it by continuous oxygen insufflation. It was now found that the injection of adrenaline in the animal after it had earlier received 3 mgm. of phenyl-methyl-aminopropane reactivated the electrical activity in the thalamus. From there the excitation was found to spread to regions in the neighbourhood of

the thalamus, finally reaching the cortex. Two minutes after the administration of adrenaline (0.1 mgm.) a seizure with tonic-clonic symptoms developed and lasted 11 minutes.

This route of reactivation via the thalamus is of interest, and has been observed in our cats in cases of exhaustion caused by large numbers of electrically induced fits. The thalamus and cornu ammonis have the highest tendency for convulsions, hence the frequency of an aura of the sub-cortical type before epileptic fits. After administering oxygen and adrenaline during a fit we were able to register frequencies up to 150/sec. with amplitudes up to 5 mv. from the medial nuclei of the thalamus and from the cornu ammonis.

If we are correct in our theory that the electrical discharge of the major fit uses up the reserves of oxygen and produces anoxia of the nervous tissue, it seems probable that the histological findings in epilepsy (including Spielmeier's sclerosis of the cornu ammonis) and those described after convulsion therapy are due to oxygen deficit. In my opinion they are not the consequence of vascular spasms as suggested by some workers, but are the result of anoxia caused by the extreme metabolic activity during the fit.

According to my hypothesis the typical course of the epileptic fit beginning with the tonic phase and followed by clonic spasms can be interpreted as follows: the tonic phase represents a maximal discharge which exhausts all reserves of oxygen and metabolites of the cells; the lack of oxygen leads to intervals of inhibition; the clonic stage indicates the end of the fit and signifies oxygen deficit; the electrical silence during the intervals and after the fit are caused by complete lack of oxygen and of other metabolites.

The prolongation of convulsions as described would appear to be another example of the facility of the central nervous system to automatize rhythmic and other motor phenomena as seen in chorea, athetosis and other extrapyramidal automatisms. Apart from the theoretical interest of the above observations, two practical *applications* arise from these experimental convulsions prolonged by oxygen and adrenaline. In the first place they give us an additional method of testing the *effect of drugs on the central nervous system*, which in the case of adrenaline, for example, was previously only possible by recording blood-pressure changes.

In the second place, the unexpected performance of the brain in prolonged convulsions suggested to me the use of oxygen insufflation, adrenaline, phenyl-methyl-aminopropane and strychnine in cases of *cerebral oedema* or similar conditions of loss of consciousness after trauma, in tumours, after operations, etc., in which revival by the usual methods has so far been without result. In some of these cases of deep coma with a respiratory rate of 40-60 and a pulse-rate of 160, good results have been obtained with this treatment combined with continuous and drastic dehydrating measures and high doses of vitamin B₁ and C.

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EYE MANIFESTATIONS IN MALADJUSTED CHILDREN.

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THE study of eye disorders in maladjusted children plays an interesting and important role in the investigation of psychosomatic problems of child psychiatry. Eye diseases in maladjusted children are frequently caused or aggravated by psychogenic factors. They are also sometimes connected with neurological disorders.

A DISTURBANCE OF THE BODY IMAGE.

Psychogenic eye diseases are due to a disturbance of the body image. By the body image is meant the picture each person has of his own body (Schilder, 1935). Emotional influences can change the relative value of the different parts of the body image. The particular desire to see or not to see an object can set up an emotional focus in the eyes. The curiosity of seeing or the horror of looking at an object is often of a sexual nature. Features of the genitals can be emotionally transposed to the eyes. The eyes therefore are a frequent phallic symbol.

Parallel with the sexual meaning of eyes and seeing there also often exists a spiritual and religious significance of eyes and the act of seeing, especially of the seeing of light. Light is frequently used in the Bible as a symbol for moral values or God. The "evil eye" on the other hand is a well-known symbol of folk lore for immoral or satanic powers.

OCULAR CONVERSION PHENOMENA.

The most common psychogenic eye disturbances are hysterical conversion phenomena. Intolerable ideas are translated or "converted" into physical symptoms. In their symbolic form they become acceptable. The operating of this mechanism is a universal human tendency which is not confined to hysteric persons, but occurs in them particularly easily and in an exaggerated form (Aubrey Lewis, 1946).

The main ocular hysterical conversion symptoms can be grouped into disturbances of movement, sensibility, glandular activity and vision (Henderson and Gillespie, 1944; Tassman, 1950).

THE BLINDING OF OEDIPUS.

One of the most moving examples for the great importance of the eyes as phallic symbols is contained in the mythological drama of *King Oedipus* by Sophocles. By drawing the attention of the modern world to this ancient myth Freud aroused worldwide interest.

Oedipus, after his discovery of his incestuous deed, tore out the golden brooches with which his mother's dress was pinned,

"And thrust, from full arm's length, into his eyes—
Eyes that should see no longer his shame, his guilt,
No longer see those they should never have seen,
Nor see, unseeing, those he had longed to see,
Henceforth seeing nothing but night . . ."

(Translation by E. F. Walling, 1949.)

EYE MANIFESTATIONS IN EPILEPSY AND MIGRAINE.

Hysteria has close relationships to other paroxysmal disorders, i.e., epilepsy and migraine. Hystero-epileptic eye manifestations deserve a special interest as epileptic attacks can be produced by emotional upset and by light stimulus. Epileptic visual auras are not uncommon.

Migraine, which possibly is related to the epilepsies, also is characterized by eye manifestations which often have a psychological origin. Visual hallucinations of flashes of light or brightly coloured spectra, scintillations or teichopsias are well known phenomena in migraine. The fundus is often normal, but retinal arterial spasm and even occlusion does sometimes occur (Graveson, 1949). Angio-spasms are due to a dysfunction of the autonomous nervous system, and this leads to the discussion of another aspect of psychogenic ocular manifestations.

OCULAR DISTURBANCES OF THE AUTONOMIC NERVOUS SYSTEM.

Emotional states act on the hypothalamus and the autonomic nervous system. If emotional experiences are related to the eyes dysfunction of the autonomic innervation of the eyes can be produced (Harrington, 1946, 1947; quoted from Tassman, 1950). If such an emotional stress is acting over a long time structural changes of the eye may occur. The above-mentioned arterial retinal spasms in migraine, the ocular changes in Raynaud's disease and above all, glaucoma, can be produced in this way.

DISEASES OF THE EYELIDS IN MALADJUSTED CHILDREN.

From the point of view of child guidance practice diseases of the eyelids are of considerable interest as they frequently have a psychological origin.

The eyelids are "mobile curtains" (Doggart, 1950) in front of each eyeball. Rising they reveal the scene of the human drama. Being the most exposed parts of the eyes they are sometimes taken as symbols for the organ of vision as a whole. If libidinous charge is pathologically concentrated at the eyes the eyelids may become irritable and may itch.

This will induce children to touch them with their fingers. The marginal glands of Zeis and Moll and the Meibomian glands in front of the posterior margins of the eyelids become in this way easily infected, especially with the *Staphylococcus aureus*. Doggart (1950) therefore pointed out that there is no doubt that children by rubbing their eyes may easily provoke external styes or hordeola. Chalazion, blepharitis or conjunctivitis also can be produced by what can be called "secondary infection of an erogenic zone."

One case of a maladjusted child will be described in whom a disorder of the eyelids played a predominant part.

CASE I.—*Bertha* (12 years 6 months. I.Q. = 119).

Problem.—*Bertha* was referred because she picked her own eyelashes and eyebrows and was very nervous.

History.—The maternal grandfather committed suicide. When *Bertha* was six years old she had two upsetting experiences. Her tonsils were removed in hospital, and when the time came for her to return home her mother was unfortunately late in fetching her. *Bertha* was terrified by the thought that her mother was not coming for her and could not overcome this shock for a long time. Her relationship to her mother was always difficult.

The other upsetting experience was the departure of *Bertha's* father, who joined the Forces. *Bertha* was emotionally very attached to her father, but she did not like his job as a hairdresser. She was particularly irritated when she saw hair left on his face when he came home from work and also when he bought a new pair of scissors. She would angrily say that this was "a waste of money." At the age of twelve years *Bertha* began to cut her eyelashes with scissors and started plucking eyelashes out. She said that the eyes were "itching."

Examination.—*Bertha's* eyelashes were almost completely missing and she had a chronic blepharitis on both eyelids. A sty was developing on one eyelid. The Terman-Merrill test showed her to be of superior intelligence. She was depressed and anxious.

Analysis.—The analysis of *Bertha's* Rorschach responses was revealing. An unusually high number of inanimate movement (m) and shading responses (FK, KF) pointed to a severe inner conflict and anxiety. Information about the nature of the conflict was obtained by the study of the content of the responses.

In not less than 11 responses she mentioned "hair" or adnexa of the skin: "A judge's permed wig," "a dog's whiskers," "a cockerel's comb," "a woman's face with

curly hair," "a man with a moustache and beard," "a man's bald head," "a funny bird with whiskers," "a terrier with curly hair," "fingers without nails," "a canary's claw with nails," "the antlers of a stag."

This showed that her father's job as a hairdresser, or for that matter her father himself, played a great role in her inner life. With regard to her references to "nails" it was interesting that she was a nail-biter.

In 6 of her responses "eyes" were mentioned: "A mask with eyes," "a dog's face without eyes," "a woman's face with eyes," "a man's face with eyes," "a man's face but I can't see his eyes," "a fat seal with eyes."

Of particular interest was one response to card III in which she saw: "A woman's face with eyes, a nose, mouth and curly hair." In card III usually two human figures are seen, which Bertha, however, completely failed to recognize. Instead of this very popular response she saw "the face of a woman," using for this response the lower two-thirds of the blot with the white space. The "legs" of the usually seen "people" were perceived as the contours of the face with the curly hair, and the middle and lower central parts of the blot as the nose and the mouth. The eyes were localized into the two small spikey prominences of the "thighs" of the usually seen human figures, details which are sometimes seen as the phallus. In this Rorschach response the genital organ seemed unconsciously to be transposed into the eyes.

The frequent emphasis on "eyes" indicated that these organs were strongly emotionally charged in Bertha. It was reasonable to assume that there was a connection between her preoccupation with "eyes" and her relationships to her mother and father. She suffered from an unresolved Oedipus situation, which produced in her a desire for expiation of intolerable incestuous ideas.

Bertha therefore took a pair of scissors and cut her eyelashes off. By doing so she not only used her father's irritating instrument—scissors—to punish herself, but also punished herself by cutting bits of hair away, hair which also bore a close connection to her father, the hairdresser. Moreover, the hair which she cut away as an unconscious substitute for castration were eyelashes, parts of her eyes, and it was her eyes which had irritated her.

Discussion.—Bertha's anxiety was due to a depressive state in a hysterical personality. The irritation of her eyelids was directly connected with an unresolved emotional relationship to her parents. During treatment she learned to realize this to a certain degree, and once she remarked: "Oh, I pulled my eyelashes out because I disliked the bits of hair on my father's face when he returned home from work." Soon after a therapeutic discussion about this remark Bertha improved. She stopped picking out her eyelashes and her blepharitis disappeared.

DISEASES OF THE RETINA IN MALADJUSTED CHILDREN.

Retinal diseases in maladjusted children deserve special attention. The human eye embryologically developed from optic vesicles which project from the primitive forebrain. The eye and in particular the retina is part of the brain. Eye manifestations in neurological disorders are therefore common and very important and are frequently accompanied by pathological changes in the retina. Maladjusted children suffering from these diseases are usually treated at paediatric or neurological departments.

One also sees, however, maladjusted children with disorders of the retina at child guidance clinics and three such cases will be described. They are of particular interest as they represent special problems.

CASE 2.—Lawrence (9 years 11 months. I.Q. = 84).

Problem.—Lawrence was referred because of antisocial behaviour. He always argued, lacked consideration, and was so aggressive to other children that he had to be excluded from school. His behaviour was so unusual that his Headmaster called him "the oddest type he had met in 20 years." The boy had one blind eye.

Family history.—Lawrence's mother was a very emotional person. The maternal grandfather was probably mentally disturbed. Lawrence's father was colour-blind. One paternal grand-uncle had an eye removed when he was 52 years old, and the mother of this grand-uncle also had an eye enucleated when she was 70 years old. No information could be obtained about the nature of their eye diseases.

Personal history.—Maladjustment: Lawrence became difficult when he began to go to school. At this time his mother went out to work and neglected him. This added to the boy's emotional strain at school which he experienced owing to his relatively low intelligence. There were also marital differences.

Eye disease: Lawrence was born with a "speck" on the left eye. When he was two years old he had whooping-cough and at that time a "cast" appeared in the left eye. At Moorfields Eye Hospital it was found that this eye had no perception of light. The right eye was healthy and its vision $\frac{6}{6}$ unaided. The nature of the illness of the left

eye was obscure but it was thought to be Coat's disease. That is a congenital vascular malformation of the retina with telangiectasies and haemorrhages.

Examination.—Lawrence was a physically strong and overdeveloped boy. His left eye was slightly smaller than the right one.

On the Terman-Merrill test he was in the dull and backward group. On the Rorschach test he showed quicker perception than would have been expected from his clinical impression. Some of his form responses were good but they alternated with poor ones. His co-operation was very poor, and the range of his determinants and quality of his responses were very inadequate.

Clinically Lawrence was very dull and unresponsive. His usual reply to questions was "Don't know." He talked very slowly, and there was an aggressive undertone in his drawn-out nasal voice. He was inadequate intellectually and emotionally, and gave the impression that his psychological difficulties alone did not fully explain his unusual behaviour.

An organic factor was felt perhaps to play a role. The possibility of a connection between Lawrence's maladjustment and the retinal disorder was considered. The question was asked, was the retinal disorder perhaps not the only pathological change of his nervous system, but was the brain involved too?

Considering the diagnosis of Coat's disease the possibility existed that Lawrence might suffer from a type of vascular malformation of the retina allied to Coat's disease, which also involves the brain. Several diseases are known in which this is the case (Elwyn, 1947). They seem to be due to a defect of mesenchymal tissue producing a "system disease."

In von Hippel-Lindau's disease for instance retinal changes are accompanied by angiomas of the brain and elsewhere, and in Osler's disease telangiectasies in the retina, brain and various parts of the body occur. In Sturge-Weber's disease evidence of a vascular naevus in the brain could be found roentgenologically by characteristic parallel lines in the X-ray picture.

On Lawrence's examination no focal signs of a pathological brain process could be detected. The X-ray examination of his skull showed nothing pathological and a search for vascular naevi of his skin also was negative.

The E.E.G. was abnormal. It showed a great excess of theta activity for the boy's age and suggested generalized cortical immaturity. No definite focal or epileptic activity was seen.

At a recent ophthalmological control examination the right eye was still found to be healthy with a standard vision unaided. The left eye had no perception of light, an early complicated cataract and the fundus showed a diffuse old choroido-rinitis. A toxoplasmosis (that is a disease caused by a protozoan parasite) was ruled out by a complement-fixation and an X-ray examination of the skull.

Discussion.—There was hereditary loading as regards proneness to nervous disorders on the side of Lawrence's mother and to eye diseases in his father's family.

Clinically the impression was gained that this boy's maladjustment was connected with his retinal disorder. It was thought to be possibly an expression of a pathological brain process. Apart from the abnormal E.E.G., however, no finding could be made to support the clinical impression, and on the strength of the E.E.G. result alone a structural cerebral disorder could not be diagnosed.

In spite of this negative result the impression remained that Lawrence's psychological peculiarities were caused by a constitutional inferiority of the brain which, however, with our present methods of examination could not be detected. A similar impression is not infrequently gained in various aspects of child psychiatry. P. Schilder (1933, quoted from M. Creak, 1951) spoke of a reaction type in maladjusted children which is due to an "undeveloped and pathologically inferior brain organization." Creak (1951), when discussing the possibility of organic factors in childhood schizophrenia, pointed out that there are clinical similarities between some cases which suffer from an organic illness with a known pathological process and cases where no organic pathological process has been found.

CASE 3.—Cyril (8 years 8 months. I.Q. = 90).

Problem.—Cyril was referred because of backwardness at school. No progress has been made in the last term and none of the new school work has been mastered. He also was rough and spiteful in his play and needed careful supervision. Cyril also had a "visual defect," and the question was raised if this affected his work.

History.—No other member of his mother's or father's families suffered from eye or mental diseases.

Cyril's early development showed no abnormalities. When he was 18 months old he fell whilst playing and at this occasion his mother noticed that he had poor eyesight. When he was six years old he developed a squint and became irritable and difficult to manage. He was examined by a specialist. The mother was informed that the boy suffered from "cerebro-macular degeneration," and that he was likely to deteriorate mentally and to die in about two years' time. The mother was stunned about this informa-

tion and lived from now on under the constant dread of Cyril's future. She gained hope when she observed that Cyril did not deteriorate as was predicted but she remained uncertain and deeply depressed.

Examination.—General impression: Cyril was normally developed physically and co-operative in his behaviour. The possibility of his suffering from cerebro-macular degeneration seemed to be very improbable. This most serious disease is characterized by rapid progressive mental failure, blindness and paralysis. There exist several forms of cerebro-macular degeneration according to the onset of the disorder. Russell Brain (1940) stated that all forms of the disease are inevitably progressive, but that the younger the child at the onset the more rapid is the deterioration. In Tay-Sachs' disease, which is the infantile form, death occurs in about two years, but in the juvenile forms the child may live up to fifteen years.

Neurological examination: There were no signs of paresis or spasticity of arms or legs. A slight divergent strabismus was present. The speech was slightly indistinct. The teeth bore resemblance to Hutchinson's incisors and Moon's molars, but the result of the Wassermann and Kahn tests were negative. The E.E.G. record was normal for the age and showed no evidence of immaturity.

Ophthalmological examination: Cyril had congenital retinal degenerative changes in the macular area of each fundus as well as some peripheral degenerative changes. The right eye was much more seriously affected than the left one. He did not require spectacles. The visual acuity was on the right eye $\frac{1}{12}$ for distance and Jaeger 1 for reading. There were also congenital abnormalities of ocular movements.

Psychological examination: On the Terman-Merrill test Cyril was of low average intelligence. He was sometimes very slow at attempting an answer and had difficulties in concentrating. On the Rorschach test the number of confabulatory responses was remarkable.

In his behaviour Cyril was friendly, but he was very sad and insecure. He also was inadequate in expressing himself. His paintings were clumsy but imaginative. Their analysis revealed that his depression was induced by his parents' depression and that he wanted to "get out of his trouble."

Discussion.—The result of Cyril's examination proved that the original diagnosis of cerebro-macular degeneration fortunately was a mistake. The fear of the gloomy prognosis had inflicted suffering on the parents, and therefore also indirectly affected the child emotionally. As soon as the parents were told about the reassuring results of the examinations their very facial expressions changed and they no longer looked so worried. Cyril's scholastic achievements and school reports also improved after this information was given to his parents.

There remained, however, an inadequacy in his behaviour. It showed itself not so much in his actions but in absence of his ability to react naturally to stimulating questions or situations. He had a certain imperception for his surrounding. There also remained the fact that he suffered from congenital retinal and macular degeneration, although of a benign form.

In spite of the definite psychological cause of Cyril's depression and anxiety it seemed possible that his maladjustment had also an organic factor. No objective proof for this could be obtained, but as in the case of Lawrence the impression was gained that in addition to the retinal changes the organization of the brain was possibly congenitally disturbed.

CASE 4.—Emma (6 years 11 months. I.Q. = 96).

Problem.—The reason of referral of this little girl was that she had "a very unusual personality." Her teacher stated that she was continually screaming out and crying about her work and extremely distressed without any apparent cause. She was so difficult that she had to be excluded from school. Emma had an artificial right eye, having had a tumour removed at 18 months.

History.—When Emma was about 18 months old her mother noticed "a little light" at the back of the right pupil. Glioma retinae was diagnosed at the Royal Westminster Ophthalmic Hospital and the right eye was immediately excised. The left eye was found to be normal. On her return home Emma was very restless and fearful. At the age of six years her beloved father died. A short time afterwards her mother broke her artificial glass eye and when trying to replace it by the spare one this also broke. This was a shocking experience for Emma, and after this happened she became intensely conscious of her lost eye. At first a new plastic eye and later a new and expensive glass eye were given to her but Emma was continuously irritated by them. She also became more jumpy and noisy and could not go to sleep without at first singing.

Examination.—Paediatric examination: Emma was a very pale little girl. The result of the physical examination was negative, including the results of a Mantoux test and blood-count. The X-ray examinations of the cranium and chest showed no evidence of a pathological process.

Ophthalmologically she had a normal socket. The left eye was normal.

Neurologically no signs of progressive organic nervous disease could be found. The E.E.G., however, gave evidence of a focal abnormality in the right temporal region. There

was also some evidence that this may be epileptic in nature, but this could not be satisfactorily cleared up.

Psychological examination: The Terman-Merrill test showed Emma to have about average intelligence. The Rorschach test showed massive confabulations, confusion and perseverations of automatic phrases.

Emma was very restless, hyperkinetic and flighty in ideas and actions. Within a few minutes she played alternatively with the dolls' house, sand-tray, Lowenfeld's mosaic and chalks. She was in a euphoric mood and sang at the top of her voice.

Emma sometimes cried dramatically and her crying seemed to have a special meaning for her. Once she said that "the houses cry through the windows." What windows meant to her became understandable when she painted a house and suddenly cut out two holes in the paper at the place where the windows were, saying "It's Emma's windows"; windows obviously were symbols of her eyes. Emma herself "cried through her eyes," she "cried her eyes out" in fear. She wanted her therapist to know about her despair, and this is the explanation for the pathetic demand with which she repeatedly greeted the therapist on her arrival: "Please say, 'crying!', 'crying!', 'crying!'."

She was intensely preoccupied with her healthy eye and her glass eye. She touched especially her glass eye frequently with her fingers. Her mother reported that she was doing this "a hundred times a day." There was no doubt that this irritation had a psychological cause.

Emma's obsessional habit of touching her eyes with her fingers was strikingly demonstrated by crayoned paintings. They showed a girl with enormous arms and hands which were outstretched as if she were crying out for help. The hands had enormous fingers. Very large eyes also were conspicuous. There seemed to be a correlation of the disturbance of her eye image with that of her arm-hand-finger image. The connecting link between both probably was the desire that what she wished to see she also wished to touch.

Eyes fascinated and frightened her, and spectacles had a similar effect. Spectacles or "eye-glasses" were for Emma as magic as "glass eyes." They represented an extension of her disturbed eye-image.

The analytical study of Emma's behaviour and work showed that at the basis of her emotional upheaval was a disturbed relationship to her parents.

Interesting in connection with this case is a study by Duke-Elder and Wittkower (1946). These authors pointed out that "the loss of one eye is not in itself a severe disability," but that "the psychological effect of the loss of one eye is out of proportion to actual physical ability."

Discussion.—This case was included in this series although the diseased eye had been enucleated because of the connection of the former retinal disorder and the present psychological state. Emma clinically had hysterical and hypomanic features.

The results of the physical examinations made it extremely unlikely that the tumour had spread into the optic nerve beyond the level at which it was severed when the excision was performed. An expanding intracranial lesion could be almost certainly excluded.

The unusual severeness of the clinical impression, however, together with the E.E.G. finding, again pointed to the possibility of an organic involvement of the brain of a kind which could not be definitely detected with our present means of examinations.

SUMMARY.

Eye manifestations in maladjusted children are an important aspect in the study of psycho-somatic problems of child psychiatry.

Psychogenic ocular disorders are caused by a disturbance of the body image. The main psychological mechanism at work is that of conversion. The main physiological process involved is brought about by the autonomic nervous system.

Psychological disorders can produce morbid thoughts, delusions and hallucinations connected with the eyes and the function of vision. The eyes can organically remain healthy, but may develop actual organic changes as a consequence of the emotional process.

An existing physical illness of the eyes facilitates the development of an additional psychogenic eye disorder. In this case the emotional disturbance can aggravate the physical eye disease.

Psychological ocular disorders can develop in all kinds of physical eye disorders, including the condition following the loss of one eye. Of particular neuro-psychiatric interest are cases of maladjustment occurring in persons who suffer from eye diseases which are part of a neurological illness involving the brain.

In this study diseases of the eyelids and retinal diseases in maladjusted children were discussed.

The psychological disturbances in children with retinal diseases in all cases described were of a serious and unusual kind. Although emotional causes could

be detected, the clinical impression was gained that they were reinforced by an additional organic factor. An abnormal E.E.G. and some criteria in the Rorschach findings in two of the three cases discussed, however, were the only objective suggestions of such a possibility. This was not enough to furnish evidence of pathological organic involvement of the brain.

In spite of this it seems possible that improvements in diagnostic examinations in the future might give objective evidence of a pathological brain organization in a number of maladjusted children with retinal changes who have shown no organic cerebral signs so far. Such evidence would also verify the clinical impression of Creak and Schilder that an organic involvement of the brain in maladjusted children probably is more frequent than is known at present.

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THE QUESTION OF HISTOPATHOLOGICAL CHANGES IN THE TESTES OF SCHIZOPHRENICS.

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IN determining the parameters of structure and function in the group of patients designated as schizophrenic, increasing stress has been laid on endocrinal function. A great deal of work is being done to clarify adrenocortical function. We are about to begin similar studies in respect to thyroid responsivity, using radio-active iodine as an indicator. The present report deals with a third aspect of the endocrine system.

The present study was undertaken to relate testicular changes such as those reported by Hemphill, Reiss and Taylor to adrenocortical and thyroid responsivity.

SUBJECTS.

Testicular biopsies were performed on the entire population (both chronic and acute cases) of the research ward at the Worcester State Hospital, with the exception of a single case.

The seventeen patients constituting the chronic part of the population had been selected from the general hospital population on the basis of the following criteria:

1. Diagnostic staff designation of the patient as schizophrenic at the time of admission.

2. Independent and unanimous confirmation, after three or more years of continuous hospitalization, of this diagnosis by the psychiatrists* of the research service.

3. Age below 40 and free of organic illness.

4. Sufficiently tractable to co-operate in ordinary test procedures.

The ten patients comprising the acute group (tested within one month of admission) were:

1. All first admissions below the age of 40 and free of organic illness.

2. Diagnosed as schizophrenic by the hospital staff. The diagnosis of schizophrenia was concurred in by the psychiatrists of the research service, although in a few cases other possible diagnoses could have been entertained, and thus the patients are by no means all of the "classical" schizophrenic type as are the chronic patients.

* Diplomates of the American Board of Psychiatry and Neurology or Diplomates of Psychological Medicine.

In this latter group two patients were eliminated. In one patient there was endocrinopathy, and in the second case operative permit was refused.

The distribution of subtypes of schizophrenia was as follows: paranoid 7, catatonic 4, hebephrenic 4, other types 8, and unclassified 2.

METHOD.

The biopsies were performed according to the technique of Charny. The sections were fixed in both Zenker's solution and formalin. Paraffin sections were stained with hemotoxylin and eosin, Mallory's connective tissue stain and phosphotungstic acid haemotoxylin.

RESULTS.

Except for slight focal inflammations in two cases there was not a single biopsy that could be regarded as pathological. Without exception all specimens had tubules, tunica propria and Leydig cells within the normal limits. Mature sperm were found uniformly and, except in one of the cases with inflammation, they also appeared to be present in normal quantity.

In about one-third of the cases there was an occasional sclerosed tubule or some thickening of the basement membrane. In no case did this exceed the frequency of such findings in entirely normal testes of the same age group.

Sperm counts could not be done routinely because of religious proscription or the patient's unco-operativeness. In the one chronic case tested the count was 160 million per c.c.

DISCUSSION.

The deviation from results obtained by Hemphill, Reiss and Taylor cannot be attributed to a difference in patient population, since the present group appears to include all types except their "chronic deteriorated."

Some of the defects illustrated and described by Hemphill *et al.* can be found in isolated areas of about a third of our cases. In the light of eight years' experience of one of us (R. S.) in examining testicular biopsy specimens at the Massachusetts General Hospital and elsewhere, it can be definitely asserted that neither the frequency nor the degree of such changes are any greater than would be expected in a similar group of entirely normal, potent males.

The absence of a single patient that had any extreme testicular defect such as Hemphill, Reiss and Taylor describe in over half their cases suggests that some other factor influenced their results. Perhaps the war-time diet or genetic factors, or a higher frequency of mumps orchitis altered the picture.

The difference reported by Hemphill, Reiss and Taylor between the schizophrenics and the other patients is statistically significant at the 1 per cent. level. We are at a loss as to how to account for this in view of our own results.

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STUDIES IN SCHIZOPHRENIA: II. ESTIMATION OF SERUM-CHOLESTEROL.

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In a previous paper (Bullock, Clancey and Fleischhacker, 1951) an attempt was made to separate schizophrenic reaction syndromes, due to diagnosable and often successfully treatable disease of known etiology, from idiopathic or cryptogenic schizophrenia. It was shown that the criteria of idiopathic schizophrenia are—

(1) *Positively*: (a) Mentally, the classical symptoms of inadequacy and inappropriateness: of thought (paralogia), of affect (parathema), to which one may add of volition (paraboulema), usually accompanied by hallucinations, paranoid ideas, etc.

(b) Physically, a slightly pathological C.S.F., due essentially to an increase of the globulin fraction.

(2) *Negatively*: the absence of generally acknowledged organic disease of the brain, or any physical disease which is known to produce such disorders of the central nervous system or the C.S.F., as mentioned under (1).

It was also suggested in that paper that these criteria, together with an examination of the serum cholesterol, might help to separate true puerperal (endocrine) psychoses, often diagnosed as puerperal schizophrenia, from puerperally precipitated idiopathic or cryptogenic schizophrenias. The true puerperal psychoses appear to be characterized by the absence of true paralogias, but by the presence of mutism or confusion or bewilderment. There is also a long-lasting increase in the serum cholesterol, and what was called a "discordant" C.S.F., viz., a definite increase of total proteins with an outspoken Lange curve, but weak turbidity reactions. The few observations published previously have been subsequently confirmed in a small number of similar cases.* The estimation of serum cholesterol carried out on 22 patients at that time had led to the tentative conclusion that in the absence of obvious endocrine disorder, or change of endocrine function due to known circumstances, including puberty, climacterium, etc., idiopathic schizophrenics have a normal serum cholesterol level. Since then, the number of serum cholesterol estimations on patients clinically diagnosed as schizophrenics has been increased to 94; 84 patients were females and 10 were males. These cases were divided into idiopathic and "potentially" schizophrenics.

1. Idiopathic schizophrenics: those who showed clinically the essential signs of disorder of thought, affect, volition, etc. In this group there were 36 such patients, most of them below the age of 40, including 10 males, the serum-cholesterol level being 160 to 210 mgm. per cent. in 29. In 7 patients—5 female and 2 male—it was higher than 225 mgm. per cent. (238—270 mgm. per cent.). All these 7 patients showed unmistakable signs of endocrine involvement (pubertal and other obesity, puerperium, ovarian cysts, hypophyseal eunuchoidism).

2. The rest (58) of the schizophrenics were incompletely examined (from our point of view), and therefore were classified as "potentially schizophrenic." According to the experience of one of us (H. H. F.), about 30 to 40 per cent. of these would not stand our tests of "idiopathic schizophrenia," but would turn out to be schizophrenic reaction syndromes. This group was complicated also by some other factors. Most of these patients were chronic ones, many older than 40 years, and

* Unfortunately, the matter could not be brought to a satisfactory conclusion since Dr. Clancey has left this hospital. It is hoped that he will be able to pursue his researches on this subject and to publish the results, including his attempts to treat such endocrine puerperal psychoses with thyroid and other hormones.

quite a number of them had had a prefrontal leucotomy, which operation is sometimes followed by an increase of the cholesterol level. (See also the tables published by Brody and others (1950).) In 27 of these cases the serum cholesterol was normal, and endocrine signs were present definitely in only 2 patients. In 31 patients the cholesterol was higher than normal (up to 300 mgm. per cent.) According to the case papers, only 5 of these latter patients showed definite thought disorder, while in 6 others paralogical thinking might have been present. On the other hand there was unmistakable clinical evidence, in at least 15 patients, of endocrine upset apart from the factors mentioned above. In principle, therefore, the results agree with our first findings, and also with those of Stenberg (1929, survey of literature). On conflicting results see also Eaton and Muntz (1947).

Assuming that in this material cholesterol is essentially an indicator, directly or indirectly, of thyroid function, the results confirm also the findings of Bowman *et al.* (1950), and of Brody and Man (1950). These authors had found, in contrast to some previous investigators, that on the whole, I^{131} uptake, protein-bound serum iodine, B.M.R. and cholesterol are more or less normal in schizophrenia, if one excludes patients whose endocrine and/or vascular system may be disturbed. While, vice versa, we have examined the cholesterol of so-called schizophrenic patients as they came along, and later on found that patients with high cholesterol levels showed, as a rule, signs of endocrine change of function, not connected with schizophrenia proper.

Apart from the 94 patients mentioned above, we examined also the sera of 23 female patients diagnosed as paraphrenia, 22 of whom had a serum cholesterol higher than 250 mgm. per cent. Paraphrenia usually occurs in the second half of the human middle age, when arteriosclerosis, hypertension, the climacterium or involution are either established or imminent. In such circumstances the serum cholesterol is often high, particularly in women, though not necessarily so often (Kountz, 1945; I. H. Page, 1945, own controls), as frequently assumed. Nevertheless, the explanation may be that in paraphrenia such factors are responsible for the increased serum cholesterol. Indeed, if one looks through the physical state of these 23 patients: age, blood pressure, conditions of the arteries, endocrine and vegetative signs, etc., there is scarcely a patient in whom one will not find one or other of these factors, and sometimes even several of them together. From this, one may conclude that the raised cholesterol level is not of any etiological significance, but essentially a concomitant as in cryptogenic schizophrenia.

There is, however, a different aspect of the problem. Paraphrenia, as a subgroup of schizophrenia may be something of a misfit. Kraepelin, although the classification was his, in his later years was not happy about it; neither was E. Bleuler (1918), nor are other authors (Henderson and Gillespie, 1950; FitzGerald, 1951.)

If one goes by the clinical signs of idiopathic schizophrenia (which are those of classical schizophrenia), paraphrenia lacks the most significant ones. The personality is well preserved, the affect is more or less adequate, and thought disturbance, if present at all, is slight. Unfortunately, no results of C.S.F. examinations are available. The main symptoms, on the other hand, paranoid ideas (sometimes grandiose), hallucinations and disturbance of mood are often met with in organic or toxic psychotic diseases. So, paraphrenia, just as schizophrenia, may be a syndrome rather than a nosological entity. What is often (much too often) diagnosed as paraphrenia, symptomatologically very closely resembles the psychoses associated with myxoedema. The psychoses of myxoedema, as Asher (1949) has reminded us recently, are most likely much more common than is generally thought, and although the patient will often look myxoedematous, this is not always the case (in cases of true, and also of secondary myxoedema). It appears highly desirable to diagnose and treat such patients as early and as adequately as possible, as chronicity of the condition, favoured by vascular and other changes occurring with advancing age, may cause irreversible damage to the brain. Asher, most of whose 14 patients were females in the higher age-group (a fact stressed by Simpson, 1949), has treated 9 of them successfully. It is well known (Clerk, 1912; Rice, 1938; Wegelin, 1926) that after the age of 50 or even earlier the thyroid undergoes frequently a marked involution. There is no doubt from our autopsy material that the number of already macroscopically pathological thyroids is rather high in elderly patients, particularly amongst women. The biochemical, supported by morbid anatomical, findings make one think that thyroid disorder may be of some importance in mental diseases other

than idiopathic schizophrenia, particularly in the last third of life (see also Annotation, *Brit. Med. J.*, 1949), and incidentally explain, at least partly, why serum cholesterol is often raised in higher age.

SUMMARY.

(1) Further examinations of serum cholesterol of idiopathic and other so-called schizophrenic diseases have shown that, on the whole, cholesterol in idiopathic schizophrenia is abnormal only when clinical evidence of a change of endocrine function is evident. These findings confirm the results of some publications, and may explain contradictions in the literature on this subject, if the concepts of idiopathic schizophrenia and schizophrenic reaction syndromes are appropriately applied.

(2) 22 out of 23 female patients diagnosed as "paraphrenia" had a serum cholesterol level of 250 mgm. per cent. and higher. The diagnostic and possibly therapeutic importance of these findings is shortly discussed.

(3) The importance of differentiating between idiopathic schizophrenia and schizophrenic reaction syndromes is stressed again. Many of the latter psychoses are often more satisfactorily treatable than, for the time being, idiopathic schizophrenia.

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SOME CLINICAL AND AETIOLOGICAL ASPECTS OF DEPERSONALIZATION WITH A CASE REPORT OF IDENTICAL TWINS.

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A SEARCH of the literature has not revealed a report of the depersonalization syndrome occurring in identical twins, although Palmer (1946) published a report of twins in which one patient was described as suffering from "all round loss of interest with some depression. . . . His thoughts . . . milled round in a ceaseless turmoil concerning his loss of contact with people and things. There was some complaint of unreality and loss of sexual desire. . . . His condition was one of distressed perplexity. The illness had come on gradually." The second patient had "tried to get his twin brother to 'pull himself together,' when one Saturday he became intoxicated and for a wager attempted bestiality. He woke up next morning feeling unutterably guilty and depressed, and rapidly developed feelings of unreality. His compelling symptom was the fear that his mind was disintegrating."

These cases appear essentially depressive and progressed to a woeful, hypochondriacal state six years later.

CASE REPORTS.

Miss Barbara and Miss Elizabeth are identical twins aged 32. Barbara is the eldest by half an hour. The twins were bottle-fed, reached the landmarks in infancy and childhood at the usual ages, both attended secondary school and both obtained school certificates. They have two brothers—the first four, the second seven years older.

In January, 1938, when 19, Barbara developed depersonalization and derealization. Elizabeth developed the condition in the June of that year, i.e., about five months later. Elizabeth was first to give up work and has been hospitalized since 1939 intermittently. The duration of her present admission is 7 years. She has been treated conservatively. Barbara was admitted to another hospital in 1949—i.e., ten years after her sister. She has had intensive E.C.T. with some subjective improvement but with the development of some secondary changes. She now has periods of normality for a few hours from time to time, but on the other hand, she feels that people do not believe what she says and that they try to avoid her. Consequently she tries to avoid others.

Elizabeth describes her state as follows:

"There is no meaning in life. I don't know what to do. It is like being in a tunnel. I can't even face minor changes in life. Nothing has any meaning. I know that these are my eyes and yet they do not seem connected to me. What I see has no meaning or feeling."

Barbara says:

"It is as if I am watching a screen. I seem big and everybody seems tiny. Things seem unreal. I feel as if my body has changed and at night I have a sensation of spreading. I feel lost within myself. When I talk it is as if I am listening to someone else. If I go anywhere or do anything I feel peculiar. I don't know what to say to my friends." She denied that she felt depressed, and said that she was merely distressed with her condition. She also remarked that "peoples' eyes seemed deadened and without meaning—like hens' eyes."

Elizabeth, although she has been in hospital for many years, does not wish to leave as she is afraid of change. She is in a non-observation ward and quite willingly does almost full time house-work—indeed in view of the nursing situation she is almost indispensable. Barbara is anxious to leave hospital as soon as possible. She has been working in the local post office as a counter clerk for the past 18 months, though continuing to live in hospital. She complained at first of difficulty in reckoning up change and remembering the various types of form with which she had to deal, but she is now quite confident about her work. In the post office she presents a normal appearance and gets on well with her

colleagues. Her symptoms of depersonalization, however, persist. She says that nothing has any meaning for her, everything and everybody appears unreal; she feels like an automaton. She asks for reassurance that her symptoms will clear up, but adds that she thinks that she will be able to carry on. She is now planning to leave hospital and live in rooms near her work. She has not been home for some considerable time, nor has she had any contact with her sister.

The onset in both cases was sudden. Barbara recalls that she was alone in the house into which the family had just moved and was looking into the fire. (Mayer-Gross (1936) strangely enough remarks that "a patient quietly reading by the fireside is overwhelmed by it"—i.e., depersonalization). Elizabeth knew of her sister's condition, worried about it and feared that she would develop it in the months before she actually did so.

Elizabeth says that she was always afraid of meeting people. She was very friendly with her sister and did not consciously feel any sense of competition. She was frightened by the onset of menstruation; she masturbated with considerable guilt and did not tell her sister of this. Her father she says was "little and quick." He did not visit either patient. Her mother she describes as "large and complaining." She feels that she ought to like her mother more as she has done more for her.

Barbara states that she was terrified by her father in early life. He drank heavily, and once threatened to cut his throat. She also has always been shy and retiring. She admits to a horror of going blind since she saw a film called "Michael Strogoff." This, we learn, was an adaptation of the novel by Jules Verne. The story (in the film) is that Strogoff is sent by the Tsar to suppress an uprising and is taken prisoner. There is an horrific scene in which he is condemned by his captors to have his eyes put out in the presence of his mother. This is duly performed by passing searing hot irons in front of them and his mother dies of shock. Unknown to her, however, the mistress of the rebel leader, by now in love with Strogoff, has arranged for him to be saved and the blinding is not properly performed. He returns to be congratulated by the Tsar.

The death of the twins' father has occurred since Barbara's admission to hospital, but this event does not have appeared to have affected either patient as far as their mental state is concerned.

Both girls are afraid of men friends, but Barbara admitted that tales of sex violence such as may be read in certain Sunday newspapers both excited and frightened her. Although she could not recall a dream on first questioning, she returned a few days later with a dream of some length recorded in detail. The dream is quite "real" but is nightmarish in character, ending: "I tried to kill a horrible worm composed of blue sleeping tablets with staring eyes and crawling all over, but couldn't kill it. I woke up in a sweat."

TEST MATERIAL.

The following psychometric tests were employed: Progressive Matrices (Raven, 1938); Shipley-Hartford Retreat Scale (used on Barbara only) (Shipley, 1940); Ink Blot Test (Rorschach, 1921); Thematic Apperception Test (Murray, 1943).

The scores in the *Matrices* are as follows:

	Set A.	B.	C.	D.	E.	Total.	Time.	Grade.
Barbara .	12	10	10	9	3	44	80'	III +
Elizabeth .	11	12	8	10	6	47	27'	II

Elizabeth just falls within the second grade. Apart from the time taken the results correspond fairly closely.

On the *Shipley-Hartford Scale* Barbara scored as follows:

	Vocabulary.	Abstract.	Mental.
Raw scores .	34	28	..
Corrected ages .	17.8	15.7	17.5

This test has as its suggested purpose the detection of organic disease, and was used as an organic aetiology has sometimes been postulated in depersonalization. The rationale is based on the finding that ability to deal with abstracts disappears before vocabulary in organic conditions. The ratio abstract ability : vocabulary

ability is expressed as the conceptual quotient, and when above 90 is said to be within normal limits. The conceptual quotient arrived at is 88 and this is interpreted as "slightly suspicious." The above tests, however, and the first Rorschach and T.A.T. on Barbara were performed within a few days of her admission, and the patient at that time was extremely upset at the necessity of having to come into hospital. This anxiety is probably enough to account for the discrepancy in times on the matrices and the lowered abstract ability on the Shipley-Hartford Retreat Scale. The latter test was repeated recently and while the vocabulary raw score remained a constant at 34, the abstract score rose from 28 to 36. The new conceptual quotient is 106, which is within normal limits, and it is apparent that other factors than organic disease can affect this ratio. A second Rorschach and T.A.T. were performed a few months after Barbara had completed E.C.T.

As far as the *Rorschach Test* is concerned, the essential points are that in all three records the number of responses is low and stereotypy is present. Before E.C.T. Barbara rejected four cards, while after treatment, like her sister, only two. Barbara's response times (T/R) and reaction times (Rt) fall after treatment, but are always within normal limits. After E.C.T. Barbara's anxiety as indicated by shading (K) and mid-line responses is relieved. On the other hand mythological responses—spirits and pixies—appear. There is a complete absence of colour (C) and original (O) responses in all three records, while the proportion of popular (P) responses is high. Shorvon (1946) mentions Rorschach findings in 40 subjects who presented depersonalization as a leading feature. His findings include reduction in colour (C), movement (M) and texture (c) responses; increased rejections of cards and a narrow range of content. Over-emphasis of form (F), anatomical (At) and rare detail (Dr) responses are also commented upon. Finally there was an orderly rigid approach to the test, long reaction times on card VI, self-recognized perseveration, and "anxiety was displayed by almost every subject."

In general interpretation of our records (Klopfer and Kelley, 1942)—and their scantiness precludes dogmatism—we may say that their general appearance is depressive; they indicate heightened self-concern; anxiety is a feature—to some extent relieved by E.C.T.—but suggestions of autistic thinking appear after E.C.T.

The *Thematic Apperception Test* was administered as described in papers by Valentine and Robin (1950). Again Barbara's reaction times fell after treatment, but on T.A.T. her rejections increased from one card to three after E.C.T. as compared with a fall on the Rorschach Test. The stories are still for the most part scanty. Rosenzweig and Fleming (1949) give the general mean of the number of words in a story as 143, with a range from 114 to 181, while here they are all under 60 words. Content is poor, and outcomes were rarely obtained without elicitation. There is a popular aspect to the stories, which are all "nice" and generally conventional. So far these features bring a resemblance to the records of depressive subjects. On the other hand, there are a number of examples of reversal of sex of the subjects in the pictures—that is to say depicted men are described as women and vice versa. This feature is frequently seen in paranoid patients. In card 17 in each T.A.T. Barbara describes a railway. This is a misinterpretation of what is usually described as the sun's rays and is undoubtedly an autism. (One of us has seen it before in the record of a deteriorated paranoid schizophrenic.)

Finally at this point we wish to mention a third patient whose case is relevant to the discussion.

Mrs. Marjorie T—, a married woman of 28, was admitted to hospital in December, 1949 (three months after Barbara), following the desertion of her husband after four years of married life, during which time she had had two miscarriages. She was depressed, bewildered, making poor contact with her surroundings and expressing mild ideas of reference. Her previous personality was described as being that of a bright, cheerful and sociable person with plenty of friends, who had no worries and no attacks of depression. She was the elder of two children, there being a brother aged 18. Her early life had been happy, and she had worked after leaving school as a seamstress, and during the war years, in the Women's Land Army. She is of average intelligence.

She received a course of electroplexy, followed later by modified insulin, after which she showed some improvement, though she continued to complain of lack of confidence.

Mrs. T— and Barbara were in constant association from March, 1950, sleeping at first in the same dormitory, and later sharing a room. Mrs. T— continued to improve over the next twelve months, but she was always somewhat preoccupied

and felt disinclined to mix with other people, apart from Barbara. In March, 1951, she obtained a post as a seamstress in a local shop, but she had to give up this work two months later as she was very slow. She herself stated that she felt tired the whole time, that things felt unreal, that she was cut off from other people and felt as though she was looking at the world through a window. She sees all the people hurrying hither and thither and it has no meaning for her. She wishes to carry on with her work, though she admits that she has no great interest in it and feels that she is doing it automatically.

DISCUSSION.

Depersonalization has been reported as occurring in numerous conditions, both organic and functional. The organic states range from epidemic encephalitis (Heuyer and Serin, 1920; Heuyer and Dublineau, 1932; Mayer-Gross and Steiner, 1921), brain tumour (Jackson and Stewart, 1899), and epilepsy (Stransky, 1922), to toxic states such as mescaline (Guttmann, 1936), and more recently dibenamine poisoning (Rockwell, 1948; Nickerson and Goodman, 1946). It has been reported as a withdrawal symptom in a morphine addict (Dicks, 1947), although here a psychogenic aetiology was supplied. It occurs in psychoneuroses (Mayer-Gross, 1936; Shorvon, 1946; Schilder, 1938), in depressive reactions (Lewis, 1934), and in schizophrenia (Galdston, 1947; Mayer-Gross, 1936). Mayer-Gross says that the depersonalization "disappears when the depression deepens or when a schizophrenic state of a paranoid-hallucinatory character follows." We have also seen it occur after E.C.T. in two patients who had not complained of it before. The first, a doctor's wife suffering from a puerperal depressive reaction with marked absence of feeling towards her baby, was treated intensively and became confused. The progress of her reaction during and after E.C.T. may be illustrated as follows: depression-depersonalization-confusion-depersonalization-depression.

The second patient, an aircraft designer with an intractable peccatiphobia, complained of unreality after three treatments. The condition again disappeared after E.C.T. was discontinued. Finally depersonalization is reported as occurring in normal individuals after emotional shock or fatigue. Inquiry among our acquaintances showed that momentary episodes were common, and that often no reason for their onset could be given.

We would point to the transitional nature of the depersonalization symptom in a number of the above conditions—the morphine addict returning to normality; the patients assailed in their current adjustments by E.C.T.; the depressive or schizophrenic before he is overwhelmed by the psychosis, when it disappears. Depersonalization here it is generally agreed is merely a symptom in a more general reaction.

There is however the special group with which we are primarily concerned in which the symptom and little else is present. Depression is denied, and over the course of years—Shorvon (1946) quotes a case of 26 years' duration—further disintegration of the personality does not take place. Because of this the suggestion is put forward that we are dealing with a new entity. Shorvon (1946) suggested the name "primary idiopathic depersonalization." Stockings (1947) compromises with the name "depersonalization syndrome." Galdston (1947) sums up as follows: "While an acceleration of the pulse beat is associated with all febrile and many other conditions it is a primary and specific disturbance in paroxysmal tachycardia. . . . There is in other words a specific nosological entity known as 'depersonalization,' and also a generic disturbance in psychic function carrying the same label which can be found associated with other specific psychopathies."

Mayer-Gross (1946) found these concepts difficult to agree with.

Our experience in the treated twin suggests that even where the symptom has persisted in apparent isolation it may well represent an unstable situation which, as in our case, may be pushed toward schizophrenic disruption, as well as, as has been conversely reported, allowing a return to normality. Fortunately our patient readjusted under a conservative regime, and has since been led to a better level of adjustment than before her treatment. In a condition where one author (Shorvon, 1946) can state, "There is therefore little or no place for the use of E.C.T. in the treatment of depersonalization," while another (Bockner, 1949) says, "E.C.T. is the treatment of choice for this syndrome," and where everything from benzedrine, nicotinic acid and calcium chloride urea to leucotomy has been used, we would merely point out that, while the symptom is generally tenacious and unalterable,

it does seem possible to produce further disintegration, and caution is therefore advisable.

In line with his attempt to describe an entity, Stockings (1947) listed a group of five symptoms: "reality disturbance, affective disorder, thought disturbance, cephalic paraesthesia, and absence of projection features." Shorvon (1946) quotes Haug (1936) as saying that the symptom of depersonalization is practically absent in paranoia, and he incorporates this statement into his list of "definite facts." It is not clear whether this is the reason that Stockings includes the "absence of projection features" in his cardinal symptoms, as Bockner (1949) goes even further and says that "it is the very absence of the process of projection that underlies depersonalization."

As paranoia (differentiated from the paranoid reaction type) is a rarity, and depersonalization as a persistent leading symptom not common, we cannot dispute Haug's finding. One of our cases (Barbara), however, does demonstrate projection features to a pathological degree, and yet undoubtedly belongs to the group that Stockings, etc., have in mind. One of us has recently seen a case with acute onset of unreality feelings three weeks previously in an intelligent housewife aged 35 who, 17 years previously, on returning to work three months after severe concussion, had had ideas of reference. We feel that a misconception has arisen which, when applied, perverts the clinical findings. It would seem to derive from a theoretical confusion which seeks to deny that "projection" and "withdrawal from reality" are consistent. In fact there is nothing inconsistent about them—a paranoid is certainly withdrawn from reality. Depersonalization, therefore, may represent a "withdrawal from reality," but it is an unwarranted assumption to say that an "absence of projection underlies it." To take the opposing view further we can see no reason why this syndrome cannot represent a form of projection—an incorrect view of reality imposed on the world. Lewis (1934) quotes MacCurdy as postulating an "affect of sudden incapacity," which is projected as part of the process when depersonalization occurs associated with depression.

Another aspect of our cases is related to the problem of *folie à deux* or psychosis of association. Gralnick (1942) defines this as a "psychiatric entity characterized by the transference of delusional ideas and/or abnormal behaviour from one person to one or more others." Brussel (1938) suggested that the basis for these psychoses was "a common heritage . . . and background . . . common environment . . . a common threat . . . and a common inherent receptivity and suggestibility." Identical twins who are reared together may be expected to share these factors. The ideas usually communicated in the condition are, however, tangible. For instance, Coleman and Last (1939) present cases where a husband comes to believe his wife's delusion that he is covered by insects; another pair shared delusions of friendship with Robert Taylor. Zabarenko and Johnson (1950) describe a case where wife and husband shared delusions that they were being poisoned by communists. Adler and Magruder (1946) describe identical twins who developed a schizophrenic-like excitement with a delusional overlay—that they had been poisoned, that their father was dead, etc. Oatman (1942) describes identical twins with identical delusional beliefs—that they were to be killed, that they had semen in their mouths, etc. Gralnick (1942), summarizing the literature in English at that time, quotes 97 cases, of which 71 displayed persecutory, 10 religious, 8 depressive, 5 grandiose and 1 pleasing delusions. Two more had ideas of infidelity. The psychoses are all delusional (usually paraphrenic, rarely manic or depressive), and concern the transmission of a false version of reality in which the prime mover believes without insight. Depersonalization, however, is not usually regarded as a delusion—although it has often been said to resemble certain types of delusion. The patient recognizes it as abnormal, is worried by it and seeks relief from it. Far from being tangible, Mayer-Gross (1936) says that it is "difficult of description by normal speech." We cannot answer the question as to whether we are dealing with a *folie communiquée* in the twins—first, the type of thought content or experience supposedly transmitted is unique; secondly, Kallman and Mickey (1946) maintain that like psychoses in blood relations should not be regarded as *folie à deux*, as the significance of heredity cannot be safely excluded; thirdly, separation did not here influence the illness of the second twin. On the other hand we may say that the basis is present for a psychosis of association as shown above, and many of the aetiological factors enumerated by Gralnick (1942) are also seen—close association, an active-passive relationship, nervous,

shy, pre-psychotic personalities in patients of the female sex, the shock and strain of seeing the (?) inducer's attack. Our patient Barbara insistently expressed the idea that people did not believe her, and this may be read as a positive wish to be believed. To complement this her sister reported her fear that she might develop the condition in the period before she actually did so. The idea that there is an active component (projection) to the illness makes the process of transmission easier to understand. The case of Mrs. T— is quoted as relevant to this issue, as after eighteen months' close contact with Barbara she too begins to express ideas of unreality in much the same words as the twin. The issue is important from the point of view of aetiology, as, apart from by bacterial or virus spread, organic aetiology is inconceivable in psychosis of association, whereas it has been postulated in depersonalization. The localization of pathology on the brain has largely been abandoned, and Mayer-Gross's proposal (1936), for example, is that depersonalization be regarded as a "pre-formed functional response." This is acceptable in so far as it goes. The implication is that depersonalization is a possible mode of reaction of the brain—and this we know to be true by virtue of the symptom's existence. Further, depersonalization is a potential mode of reaction of *any* brain—and again the clinical evidence is supportive, as it occurs in normal people and in a wide variety of pathological conditions. In fact we are only playing with words, for any symptom may be produced in any subject given the right pathological setting, and in a wide sense any symptom is a "pre-formed functional response"—a possible way for the body to react. Moreover it is not the knowledge that a symptom is "pre-formed functional response" that is important. (Sleep, for example, is such a response.) It is the pathological setting—the conditions for the release of the symptoms that count. (Knowing that a subject sleeps at night tells us little of his chances of developing hypersomnia). In our view the conditions for the release of the depersonalization symptom are psychogenic.

Many of the psychological theories concerning the condition have been criticized as being incomplete (Mayer-Gross, 1936), and some recent additions appear frankly sterile. Galdston (1947) suggests that the "ego is a functional entity without embodiment. The ego is related to the id and to the super-ego as 'the spinning is to the spinning top' . . . or as 'the circulation to the circulatory system' . . . The ego is engendered by the interaction of the id and the super-ego and its function is to integrate both. . . . Disruptive factors that can affect the integrative function of the ego may stem from the id or the super-ego or both. . . . Depersonalization is a degradation of the integrative function of the ego . . . perceived and appreciated by the ego." As a corollary of the above he suggests that depersonalization is present in practically every case except those of sudden onset and fulminating development. He also suggests that depersonalization arises from a functional weakness of the super-ego, and regards it as a benign form of schizophrenia (where the weakness is in the id). Mayer-Gross (1936) points out that theoretically speaking one would expect depersonalization to be present much more often than it is. It remains a fact that it is not present in "practically every case." Galdston only gives a brief report of one patient to illustrate his argument. This patient, a female, terminated her treatment saying: "Doctor, there is nothing wrong with me that a good man couldn't put right." There is no follow-up reported.

It seems to us that all this is tantamount to saying that when the subject is healthy and "personalized" the ego is adjusted; when depersonalization is present it is maladjusted. Depersonalization is therefore a disorder of ego function—and this finding we feel might have been arrived at in a less round-about way.

Miss Searl defended the analytic school from the criticism that "the disagreement among them is discouraging" (Mayer-Gross, 1936) with an oft-quoted, but not always acknowledged review, designed to show that their attitudes are complementary. The salient points are that there is little or no breast-feeding, severe physical punishment for viewing or exhibiting in the Oedipus situation in defiance of restraining looks, a consequent increase in the scrutinizing tendency, and an attempt to escape punishment by assuming the immunity of inanimate objects. Lifelessness is compensated for by extreme activity and erotization of thinking identified with the frustrating parent. Bergler (1950), who is quoted by Miss Searl, has recently written extending his earlier view that the "anal-exhibitionistic repressed wish is warded off with pleasurable self voyeurism; that defence is prohibited by the inner unconscious with the result that a secondary unconscious defence is

installed: 'I don't peep at myself, I just mournfully observe my sickness'." He now believes that a scotophiliac exchange mechanism is the basis for depersonalization, and that the specific answer for the typical anal variety of exhibitionism hinges on beating phantasies. Depersonalization, he says, "represents one of the many attenuated end-results of 'a child is being beaten' phantasy in so far as it is being executed with scotophiliac means." And again: "In cases in which beating phantasies are combined with extensive scotophiliac tendencies depersonalization is used as a typical defence mechanism." Bergler expresses therapeutic optimism, which in this condition is not general in analytic circles.

We note the relationship of his finding to our patient Barbara's fear of blindness arising from her experience with the film, coupled with the onset of her illness when she was looking into the fire. We feel that the circumstance of onset—the psycholeptic attack (Muncie, 1948)—is worthy of investigation in these cases. One of us recently saw a case where a woman who at that time thought that she was behaving quite normally heard her husband say to her, "Why are you so distant with me?" She fainted and awoke depersonalized. We feel that Shorvon's results with ether abreaction were not due merely to physiological excitation, or the reversing of a hypothetical state of low tension (Janet, 1922), but to touching off relevant psychogenic material. In each of the cases he quotes (1946) the circumstance of onset was used to produce abreaction, although he himself does not make this point. In this respect Muncie (1948) notes that depersonalization is often the aftermath of vivid experience, and Fenichel (1945) says that it is a defence against excitement. We would relate the circumstance of onset to an underlying psychopathology, possibly as suggested by Bergler, with the resultant release of a symptom which may have organic concomitants. These, however, must be secondary if we are to allow that the condition may be transmitted by association.

SUMMARY.

Case-histories of identical twins suffering from depersonalization are presented with relevant psychometric material. The case of an associate of one of the twins is also described. The diagnostic value of the Shipley-Hartford Retreat Scale is questioned. The distribution of depersonalization as a symptom and its transitional nature are discussed. The effects and possible dangers of treatment are examined. The concept that projection features are necessarily absent from the depersonalization syndrome is criticized. The question as to whether depersonalization can be transmitted in psychosis of association is examined in relation to the case-material. Some aetiological theories are reviewed, and the importance of the circumstance of onset is stressed.

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TEACHING AIDS IN CLINICAL PSYCHIATRY.

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THE effective teaching of Psychiatry to medical students remains a formidable problem for many reasons apart from the actual methods employed by the teacher. Allocation of adequate time to the subject, the attitude of other teachers and students towards it, the facilities provided by local hospitals, clinics and other institutions alike contribute to the difficulty in establishing Psychiatry as a major subject within the medical curriculum. It is with the problem of teaching method alone that this paper wishes to deal: first to outline the inherent difficulties commonly encountered; secondly to describe the design of structures and equipment found useful in overcoming these difficulties in some measure; and thirdly to point the way for possible future development.

PRESENT LIMITATIONS.

Present clinical teaching in psychiatry is modelled upon clinical medicine, with the demonstration of the typical case at the bedside or in the lecture theatre as the central theme. There are many reasons why traditional methods, found so successful in the one sphere, are much less so in the other. Some of these will now be discussed.

i. Many psychiatric patients are unsuitable for demonstration before a group of students. Some patients will object, others will withhold important information about their private lives, others again (the exhibitionists) will distort information, exploiting the situation for personal gratification. While the average patient can tolerate his body becoming public property, he wishes to retain his mind as a private possession. This objection applies principally to most cases of neurosis, to those exhibiting emotional problems with psychosomatic disorder, to sexual deviates, and to some psychopathic personalities.

ii. The elusive quality of many symptoms and signs in psychiatry presents a major problem in formal demonstration. Often the symptom is transient; rarely can it be demonstrated as if it were, say, a cardiac murmur for anyone to hear at almost any time. Often it disappears on close scrutiny or in the actual process of demonstration. Objective commentary disturbs, perhaps annoys or embarrasses the patient so that only this secondary state is observed.

iii. The long and variable course of most psychiatric disorders renders the introduction of the time dimension in demonstration virtually impossible except by second-hand reporting. To report upon the patient rather than demonstrate him to students introduces an element of unreality which often leads on to frank incredulity. Students will simply not believe what they are told, for it is already too far removed from their everyday experience—even from their experience as medical students immersed in the clinical study of other types of case-material.

iv. Objective commentary by the clinical teacher upon his own method is not always a pleasant task, nor an easy one. If the natural tempo of the psychiatric examination of the patient is to be preserved, the teacher cannot carry out a running commentary nor can he readily invite questions from his students. Nor is it altogether satisfactory to postpone all discussion of the case until after the examination, when the vividness of the demonstrated material has been lost and cannot be recaptured; and it is impossible to demonstrate the variety of techniques which may be employed to elicit the same kind of information in different patients. The student can learn only in a most limited way what is in the mind of the teacher

as he proceeds to examine the patient: what system of investigation he is adopting in the particular case; what diagnostic categories are being considered; what methods of disposal are open before him. For the most part the student is ignorant of the significance of pauses, changes in emphasis and subject, and other finer points of interview technique. These difficulties of commentary are particularly evident when specific test procedures for intelligence, memory, attention and so forth are being demonstrated, and above all in therapy.

v. It has been rightly pointed out by Strauss (1947) that "Psychology is the most abstracting (not abstract) of all the sciences. Any and every psychological formulation is little better than a parable, a simile or a metaphor." It can also be the most disturbing to the earnest newcomer, and his confusion by the subject-matter or a desire to escape from it are ever-present evils which must be avoided by the good teacher. The answer is for him to present the clinical facts with great simplicity and directness, to select the case-material so that the least disturbing is presented initially, and to graduate succeeding demonstrations within a planned and prepared clinical course. Such planning and preparation cannot easily be carried out within the traditional framework of clinical demonstration, and it is in this connection that the value of the procedures to be described will be apparent.

POSSIBLE SOLUTIONS.

The one-way screen is a window of glass which permits observers to see without being seen; thus it can be adapted for teaching purposes in the psychiatric interview, with the patient and doctor on one side and the student observers and their commentator on the other. One-way screens of different types have been used in psychiatric research and teaching for some time. A crude type of screen is described by Gesell (1947); it consists merely of a piece of gauze mesh let into a door, and behind it the observer has to sit in silence and darkness. A simple device such as this works satisfactorily enough, and it is an unfortunate fact that the more ambitious type of screen requires a great deal more elaboration to get better or even comparable results.

The observers, seated in the room next to that in which the interview takes place, require some means of hearing what is going on, and this is most conveniently accomplished by a sound reproduction system—a microphone, and its amplifying channel and loudspeaker. With the addition of recording apparatus a permanent record can be made of the interview.

Sound recording of psychiatric interviews has been developed as a teaching and research technique in recent years, reports having appeared in the literature both in this country—Bierer and Ström-Olsen (1948), Oldfield (1949)—and in the U.S.A.—Brody, Newman and Redlich (1951), Redlich, Dollard and Newman (1950), Rodgers (1946). One of us (W. M. M.) had been impressed by the possibilities for psychiatry of modern high-fidelity recording during the last war (McLaughlin and Millar, 1941). The views expressed by Kubie (1947, 1948) on the importance of records and films as a means of obtaining more permanent and observable data for teaching and research in psychiatry acted as a timely stimulus when the present Department of Mental Health at Aberdeen was being planned. This department has now been constructed, and two rooms have been designed so that the maximum use can be made of different types of sound-recording equipment, a "live" amplification system and a "one-way" vision screen.

A basic principle may be enunciated at this point, in so far as it is undesirable to use the one-way screen for eavesdropping on the patient; he should always be told that the interview can be seen and heard by students or other doctors in the next room. One might think that this means the same thing to the patient as having the observers in the room with him, but in fact this is not the case; so long as they are unseen and unheard the knowledge of their presence changes the quality of the interview surprisingly little. Questioned about this afterwards, patients usually say that they forgot about the one-way screen within a minute or two, and opening up the interview may well prove more embarrassing to the psychiatrist than to the patient. From this principle follows the corollary, there is no need to disguise the screen or microphone; and hence any "disguising" of those is in the nature of camouflage rather than concealment. The screen and microphone therefore should be made to appear as innocuous as possible, but no attempt at complete concealment is necessary.

These features are now considered in some detail, because apparatus of this sort gives disappointing results unless proper care is taken in its construction. The aims to keep in mind are, first, that the interview should be unembarrassed by technical intrusions; and second, that the observers should be able to see clearly and hear without strain.

TECHNICAL CONSIDERATIONS.

The "One-way" Screen.

Given sufficient space, one imagines a system based on these lines: a unit composed of interview room, small recording room, and auditorium or viewing-room. The auditorium would have tiered seating for 20-40 persons, and the screen permit vision of the entire interview-room. The whole unit would be sound-proofed from the rest of the building, and its individual sections sound-proofed from each other.

In practice, however, it is usually a matter of adapting two existing rooms, and the main item is the screen of "one-way" glass which is let into the party wall between the interview-room and the viewing-room. This must be of adequate dimensions—say 6 ft. $\times$ 3 ft. 6 in.—and the lower edge should not be more than 2 ft. 6 in. from floor level if the viewers are to be seated. A screen of this size will comfortably accommodate a group of 8-12 students without tiered seating; in our experience this is the best size of group for clinical teaching. It is usual to mount the "one-way" glass flush with the viewing side of the wall, and to help in sound-proofing a piece of plate glass is similarly mounted on the interview-room side of the wall.

Two types of "one-way" glass are currently available—one which presents a black surface, the other a mirror surface, as seen from the interview-room. Both depend on absorption of re-entering light and require differential lighting—that is, the viewing-room must be heavily shaded or in near-darkness, and the interview-room brightly illuminated. The shading of the viewing-room, however, need not preclude the use of a miniature slide projector; this is a useful "visual aid" in the demonstration of psychological test procedures. As an example, the Rorschach test plates may be projected on a small screen on a side wall of the viewing-room for the students to refer to, while the test is in progress in the interview-room.

Both types of glass appear to possess approximately the same optical efficiency, and which one uses is largely a matter of individual preference. The windows of "one-way" and plate glass form between them a sort of cupboard within the thickness of the wall, and it can in fact be used as such or otherwise made to fit in with the general decor.

A bright, sunny room can be viewed satisfactorily by daylight, but in most circumstances reinforcement by powerful artificial lighting is necessary, since ordinary standards of room illumination are quite inadequate to withstand the loss in intensity caused by the screen; diffused reflected light from the walls and ceiling is preferable to direct lighting. If fluorescent lighting is utilized, the "warm white" type of tube assists in correcting for the greenish coloration apt to be present in plate glass. In this case, diffusing louvres are desirable over the fluorescent tubes, and the chokes should be installed outside the room to avoid mains hum interfering with the sound system. Whatever type of illumination is used, light-coloured walls and furnishings will be an advantage.

The Sound System.

This falls naturally into two divisions—sound reproduction, by which is meant the relay of "live" sound from room to room; and secondly, sound recording. The second may include the first, but it is as well to have separate channels for each.

In considering the equipment required, it is essential to start with the room in which the sound is produced. This is just as important as the rest of the acoustic apparatus, and strivings after perfection in equipment will be frustrated unless the "studio" equals the quality of the microphones, amplifiers, etc. The interview room must therefore be submitted to a thorough acoustic damping treatment, and when adequately treated the room should have no perceptible reverberation-time. It is also important that the two rooms should be sound-proofed from each other, as otherwise acoustic feed-back from loudspeaker to microphone will occur at ade-

quate listening levels. Some useful information and references are given by Shears (1951); but again a compromise is necessary, and it is better to accept something a little short of ideal rather than have the patient suspect that frantic efforts have been made to reproduce his voice naturally. Similarly the viewing-room must not be neglected, as the sound is to be reproduced there; and the quality of the reproduction will suffer if the room contains a lot of reflecting surfaces.

So far as microphones are concerned, our first intention was to conceal these—the concealment being merely to relieve the patient of the embarrassment of having the instrument in front of him. Finally, however, the idea was abandoned, and for adult interviews we use a free-field moving-coil microphone mounted normally but as inconspicuously as possible. One reason for this decision was that we found it impossible to retain the highest fidelity results from a concealed microphone.

Getting the microphone leads through the wall in any neat fashion presents something of a problem, solved in our case by a conduit-box. This is a small aluminium box which slips into place like a brick into a hole made for it in the party wall. It has several standard screened jack-sockets connected from side to side, so that the microphone leads simply plug "into the wall." The conduit-box can also be used for intercom equipment, and adapted to transmit low-tension currents, e.g., to actuate from the interview-room a kymograph signal-marker on the observers' side; tubes are also mounted through it so that a pneumograph and sphygmomanometer in the interview-room may record in the viewing-room for experimental purposes.

We have now traced the sound path to the point where signals enter the amplifier. The amplifier must be virtually distortionless and matched to the microphone; a good signal-noise ratio is more important than high gain, and its output should be matched to a properly mounted loudspeaker of good quality. For information on loudspeakers and their mounting Briggs' (1949) book should be consulted.

In this connection it is worth while considering the merits of a "stereophonic" sound system. An objection to the usual monaural (single-channel) system is that direct and reflected sounds are mingled inseparably so that the listener cannot distinguish between voice sounds picked up by the microphone direct and those reflected to it. A more natural and lively reproduction of the interview can be obtained by mounting two similar microphones back-to-back on the desk; each is led to a similar amplifier and loud-speaker, and the speakers are set up on the screen wall of the viewing-room at either side. If the gain in each channel is adjusted to equality, the conversation appears to have a three-dimensional quality, as the voices of interviewer and patient come from points which correspond to their actual positions.

Our installation has entirely separate channels for the following:

i. Live sound reproduction, i.e., listening to an interview in progress. For teaching purposes this needs the attention of two staff members, one to conduct the interview and one to act as commentator with the students. The commentator can momentarily suspend proceedings by turning down the amplifier to allow him to explain things to the students.

ii. Tape recording: For interviews where some permanent record may be desirable, the microphone is switched to the tape recorder, and the interview can also of course be heard by one of the monitoring systems. Recordings are made in this way of any interviews likely to be of special interest, and these are used to illustrate the course of lectures in systematic psychiatry; they are also helpful in staff conferences from the dual viewpoints of study of the patient, and study of interview technique. Also, special features can readily be built up and edited by joining sections of tape. This is especially valuable in order to compress an interview; if, for example, one wishes to illustrate some points out of it and discard the rest, they can be extracted from the tape reel, edited and supplied with a commentary. Thus compressed, the recording can be dubbed on to discs with no loss of quality, in a convenient form for filing and reference.

iii. Direct disc recording is used to make the permanent records which we wish to retain. We use it now only to make dubbed records; interviews, etc., are recorded first on tape, and afterwards edited and dubbed to discs as required. The record is available for replay immediately on any orthodox turntable, and the 12-in. record at the conventional speed of 78 r.p.m. has a playing time of $4\frac{1}{2}$ minutes each side. Microgroove recording can increase this to about 17 minutes per side, but the technical difficulties become rather more formidable.

Any number of copies may be made by repeated dubbing, or by impressions from a master disc; a pleasing feature of these records as compared with commercial pressed recordings is their low surface noise. For more detailed information on disc recording the reader is referred to Briggs (1950).

Only very brief mention has been made of the technicalities involved in a satisfactory one-way-screen and sound recording system, but the authors will be pleased to give full details on personal application.

DISCUSSION.

A set-up such as we have described will be found readily adaptable to the teaching requirements of the unit. In our own case we have found it particularly successful with the groups of medical students taking a short intensive course in clinical psychiatry in their fourth year. On the first day of this course they are given demonstrations of psychotic and psychoneurotic patients, broadly to illustrate their differentiating features. On the next few days there follow demonstrations of common psychiatric reaction-types, such as anxiety, depression, and hysteria; and a valuable feature is the demonstration of a diagnostic interview. By this we mean a session with a patient referred for consultant opinion for the first time. The students find it particularly rewarding to observe the psychiatrist review the history, elicit signs and symptoms, and generally conduct the interview, while at the same time the commentator is "reading his mind," and interpreting to the students such points as differential diagnosis and the problem of disposal. Later in the course, demonstrations are given of psychological test procedures, children's play therapy, examples of organic impairment, and the follow-up of patients discharged from mental hospitals. In the course of these sessions the students have the opportunity of watching a number of psychiatrists at work, but the danger of their becoming confused by this variety is offset by the continuity preserved by the commentator.

On occasion a "set piece" may be presented, the aim being to provide a rapid but comprehensive introduction to the whole field. In these demonstrations the case is presented from several different viewpoints. The patient is examined by the psychiatrist (in effect, an "initial interview"), while the commentator interpolates in accordance with a pre-arranged plan. This is followed by a report from the psychiatric social worker on the interview with the relatives and the home visit. The case presentation is further amplified by the psychologist's account of the test procedures carried out; and finally the doctor who has had charge of the patient's care (ideally to the point of cure) gives an account of his treatment plan and the patient's response to therapy up to the present time.

The recording apparatus itself may of course be employed separately in the teaching of systematic psychiatry, as a clinical aid, in research and in other ways. For instance, a library of discs may be built up consisting of typical case-material, illustrative examples of mental mechanisms, and classic mental signs. Serial recordings of the same patient taken over the course of treatment and in follow-up are of value as an objective means of assessing progress. In research, it is clear that we have an instrument of great value in that psychiatric data are rendered permanent, and set down for detached observation by any number of observers. Other uses suggested include the instruction of trainee psychiatrists by playback of interviews and discussion of their own technique; and it has also been suggested that members of the faculty might care to listen to recordings of their own lectures as delivered to their students.

SUMMARY.

The traditional methods of teaching in clinical medicine are found to be unsuited to the teaching of clinical psychiatry; the problem is examined, and a possible solution offered in the exploitation of the "one-way" screen and sound system. Technical details are given for the construction and use of this equipment, and suggestions made as to the most rewarding methods for its use in teaching. The possible future development of these techniques is discussed.

We wish to acknowledge our indebtedness to Professor Rex Knight and Dr. (now Professor) F. V. Smith of the Department of Psychology, who, already experienced in this field, gave us much valuable advice in the initial stages; and

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THE TREATMENT OF MENTAL DEFECTIVES WITH GLUTAMIC ACID

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INTRODUCTION.

BECAUSE of the professional and lay interest in the potential value of glutamic acid in the treatment of mental deficiency the present study has been conducted.

From the section of Lennox Castle Institution, which is devoted to the training and treatment of Male Juvenile Mental Defective Delinquents, 30 patients were chosen. Half of these were treated with glutamic acid and half used as controls.

The analysis is based upon comparison between experimental and control group rather than between paired individuals. As may be seen from the table, the two groups are very similar. There is no significant difference in the age, intellectual capacity, social background or environment.

Comparison of Groups.

	Experimental group.	Control group.
Average age	12 yrs. 2 months	12 yrs. 6 months
Average residence in the Institution	10 months	11 months
Average I.Q.	62	64
Average practical ability	76	76

Throughout the entire period of investigation experimental and control cases were inmates of the same Institution, receiving the same training, care and diet, the latter being prepared in the central kitchen, and attending the same Institution school. In that way we tried to obtain an adequate " background " for our investigation.

All these boys were without signs of organic brain lesion. There were no epileptics among them.

The fact of institutionalization indicates that they were maladjusted and in need of regular supervision. They were delinquents or presented serious behaviour difficulties at home.

All are educable, and the majority leave at the age of sixteen for employment under ordinary conditions.

TESTING.

To assess their I.Q., Cattell Test IA was given before the beginning of treatment and Cattell Test IB after treatment, since the norms for Form IB, which is an equivalent for retesting purposes, make allowance for practice effects following testing on Form IA.

At the same time they were tested for P.A. (practical ability) with the Passalong Test.

METHOD OF ADMINISTRATION OF GLUTAMIC ACID.

Glutamic acid was administered in tablets (Parke, Davis & Co.), each containing 0.5 grammes ($7\frac{1}{2}$ grains) of the naturally occurring dextro-rotatory substance. The daily dose was 9 gm. (6 tablets *i.i.d.*) for the first 4 months and 12 gm. (6 tablets *q.i.d.*) for the subsequent 6 months. There were no side-effects. On no occasion has a boy refused to take the glutamic acid tablets or shown any gastric distress.

The snag is the high cost of treatment, the cost of keeping each patient supplied with glutamic acid being approximately £1 per week. For that reason the application of glutamic acid had to be confined to a small group of 15 mental defectives.

RESULTS.

Four out of fifteen boys treated with glutamic acid for ten months gained in I.Q. from 8 to 11 points, while none of the control boys showed a gain of more than 2 to 3 points, which is not beyond the experimental error in measurement.

The gains in P.A. (practical ability) measured by the Passalong Test were not so marked; the control group appeared to gain about as much as the experimental group. The gains may be, therefore, practice effects.

Mental deficiency is first and foremost a social concept, behaviour being of paramount importance as regards fitness for normal life. In this investigation the social aspects have been noted; i.e., the general behaviour in the villa where the boys live and the progress at school or work in our occupation centre and simple domestic routine work.

In 8 of 15 boys in the experimental group there was a definite improvement in general adjustment observed by myself, the teachers and male nurses. Their behaviour was improved, they were more alert, self-confident and showed more interest, while none of the control boys showed such marked changes.

SUMMARY.

Fifteen feeble-minded, maladjusted boys were treated with glutamic acid for 10 months, with an I.Q. before treatment, ranging from 54 to 76 (only one boy had an I.Q. of 48) and ranging in age from 10 to 15 years. All these boys were without signs of organic brain lesion. There were no epileptics among them. In 8 of these 15 boys there was a definite improvement in general adjustment; 4 out of these 8 boys gained in I.Q. from 8 to 11 points, while the improvement of the control boys was negligible.

I am indebted to Dr. J. T. Curran, Medical Superintendent of Lennox Castle Institution, for permission to conduct the treatment, and for his interest in the experiment and his valuable advice. My thanks are also due to the staff and the teachers in Lennox Castle Institution for their assistance.

Boys on Glutamic Acid Treatment.

Patient.	Admitted.	Age at beginning of treatment (Jan., 1950).	Previous history (before admission).
1. R. S— .	17.x.49	15 years	Indecent assault on little girls.
2. W. E— .	25.x.48	11 "	Stealing and wandering.
3. A. C— .	16.viii.48	15 "	Stealing. Broken home (father in jail, mother dying of T.B.).
4. J. G— .	29.xi.48	10 "	Neglected. Parents divorced.
5. R. B— .	25.x.48	13 "	Stealing. Truancy.
6. A. M— .	11.xi.48	12 "	Beyond home control. Truancy, wandering.
7. D. T— .	26.x.49	14 "	Stealing, truancy. (Head teacher)—violent and aggressive, not amenable to discipline. Evil influence.
8. E. F— .	7.xi.49	11 "	Stealing.
9. A. F— .	28.vi.49	14 "	Stealing.
10. J. D— .	26.xi.48	13 "	Stealing, truancy.
11. R. McD— .	25.ii.49	11 "	Beyond parental control.
12. T. F— .	28.vi.49	12 "	Stealing.
13. W. McG— .	25.vii.49	12 "	Malicious mischief.
14. A. M— .	5.iv.49	10 "	Housebreaking with malicious mischief and fire raising.
15. J. C— .	10.i.49	10 "	Stealing.

Control Boys.

Patient.	Admitted.	Age, Jan., 1950.	Previous history (before admission).
16. W. C—	3.iii.47	12 years	Theft and malicious mischief. Truancy.
17. W. B—	19.vii.48	12 "	Beyond home control. Malicious mischief.
18. W. C—	28.xi.49	15 "	Beyond home control. Stealing, truancy.
19. D. F—	14.x.48	13 "	Neglected. Illegitimate.
20. R. C—	19.ix.47	11 "	Orphan.
21. J. McD—	20.viii.47	13 "	Neglected. Beyond home control.
22. D. S—	9.xi.49	13 "	Theft and malicious mischief.
23. W. A—	29.xii.48	15 "	Theft, truancy.
24. H. S—	17.vi.49	10 "	Eight convictions for burglary.
25. J. McI—	24.xii.48	14 "	Truancy.
26. A. W—	14.xii.49	13 "	Truancy. Beyond home control.
27. J. H—	15.xii.49	13 "	Theft, truancy.
28. D. H—	28.xi.49	13 "	Choreiform movements.
29. W. W—	21.xi.49	12 "	Orphan.
30. W. O'R—	10.i.50	10 "	Theft.

Boys on Glutamic Acid Treatment.

Patient.	Before treatment I.Q., Cattell IA.	After 10 months' treatment I.Q., Cattell IB.	Before treatment P.A. Passalong Test.	After 10 months' treatment Passalong Test.
1. R. S—	58	67 (+ 9)	61	89 (+ 28)
2. W. E—	63	64 (+ 1)	86	86 (same)
3. A. C—	56	64 (+ 8)	65	65 (")
4. J. G—	67	78 (+ 11)	75	82 (+ 7)
5. J. D—	62	67 (+ 5)	72	74 (+ 2)
6. R. B—	63	65 (+ 3)	73	76 (+ 3)
7. A. M—	71	80 (+ 9)	70	70 (same)
8. D. T—	62	65 (+ 3)	74	83 (+ 9)
9. E. F—	75	75 (same)	80	80 (same)
10. A. F—	48	48 (")	79	90 (+ 11)
11. R. McD—	76	76 (")	65	80 (+ 15)
12. T. F—	54	54 (")	88	90 (+ 2)
13. W. McG—	63	65 (+ 2)	78	78 (same)
14. A. M—	58	58 (same)	99	107 (+ 8)
15. J. C—	55	54 (— 1)	78	81 (+ 3)

Control Boys.

Patient.	I.Q., Cattell IA.	I.Q., Cattell IB.	Passalong before.	After 10 months.
16. W. C—	78	77 (— 1)	89	99 (+ 10)
17. W. B—	61	60 (— 1)	86	86 (same)
18. W. C—	69	68 (— 1)	81	87 (+ 6)
19. D. F—	50	51 (+ 1)	45	55 (+ 10)
20. R. C—	60	60 (Same)	70	88 (+ 18)
21. J. McD—	47	47 (")	72	73 (+ 1)
22. D. S—	61	61 (")	66	70 (+ 4)
23. W. A—	57	57 (")	61	70 (+ 9)
24. R. M—	59	58 (— 1)	60	63 (+ 3)
25. J. McI—	61	61 (Same)	60	71 (+ 11)
26. A. W—	85	87 (+ 2)	106	109 (+ 3)
27. J. H—	69	72 (+ 3)	103	107 (+ 4)
28. D. H—	65	65 (Same)	90	91 (+ 1)
29. W. W—	64	66 (+ 2)	91	91 (Same)
30. W. O'R—	75	73 (— 2)	67	65 (— 1)

Boys on Glutamic Acid Treatment.

Patient.	Behaviour change.
1. R. S— .	Was very timid before treatment. Is more alert and self-confident ; can hold his own better.
2. W. E— .	Behaviour much improved, more social ; can dress without supervision and does little jobs in the ward.
3. A. C— .	More alert and self-confident. Good and willing worker in the ward. Best boxer in the ward. In football team.
4. J. G— .	More alert and self confident. Can hold his own now. Keen to learn.
5. R. B— .	No improvement in behaviour ; still overactive and lacks concentration.
6. A. M— .	Behaviour improved. More alert, tidier ; shows more interest in his work and at school, still wanders.
7. D. T— .	Behaviour always was good since he was admitted to Lennox Castle Institution. Developed a sense of humour.
8. E. F— .	Still lacks energy, is not interested in any work or games.
9. A. F— .	No change in behaviour.
10. J. D— .	Ditto.
11. R. McD— .	"
12. T. F— .	"
13. W. McG— .	Behaviour much improved ; more alert and interested in his work. Works in the garden of his villa.
14. A. M— .	Improved ; more alert and shows more interest.
15. J. C— .	Behaviour improving ; developed a sense of rhythm in the percussion band. Very good at marching.

Patients who showed Improvement after Glutamic Acid Treatment.

Patient.	I.Q.	P.A.	Behaviour.	Before treatment.	
				Age.	In Lennox Castle Institution.
1. R. S— .	+	+	+	15	4 months.
2. W. E— .	—	—	+	11	1 year 4 months.
3. A. C— .	+	—	+	15	1 year.
4. J. G— .	+	+	+	10	1 year 1 month.
7. A. M— .	+	—	+	12	1 year 2 months.
13. W. McG— .	—	—	+	12	6 months.
14. A. M— .	—	+	+	10	4 months.
15. J. C— .	—	—	+	10	1 year.

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Part II.—Reviews.

Analytical Biology. By G. SOMMERHOFF. London: Oxford University Press, 1950. Pp. 208. Price 21s.

The invasion of psychology by cybernetics is making us realize that the ordinary concepts of psychology must be reformulated in the language of physics if a *physical* explanation of the ordinary psychological phenomena is to become possible. Some psychological concepts can be re-formulated more or less easily, but others are much more difficult, and the investigator must have a deep insight if the physical reality behind the psychological phenomenon is to be perceived. Prominent among such concepts are those related to "purpose," "adaptation," "co-ordination"—the words that express some co-operation towards a goal. Sommerhoff has attempted to re-formulate them in purely physical terms. His study is worth while, for these concepts are among the most fundamental in all psychology.

As a physicist, Sommerhoff is accustomed to using concepts like "polarization" and "entropy," which, though too complex to be defined in a few words, are none the less defined with full precision and objectivity. Though physicists may dispute about polarization, they are never in any doubt as to what they are talking about. Compare this certainty with the state of psychologists disputing about adaptation! Sommerhoff has attempted to define this concept of "adaptation" in a form that shall meet to the full the psychologist's insistence on its peculiarity, while at the same time meeting to the full the physicist's demand for precision and objectivity. In this he has been, I think, successful. He has shown clearly that such a definition is possible, and he submits one that has been constructed with great care. I shall not quote it here, for it would be meaningless without its context; I will merely say that he gives it in two forms, first in plain English for practical use, and then in mathematical symbolism to show that the definition is both objective in application and freed from all unwritten implications.

His definition is of peculiar interest to me as I am one of those* who have also proposed a definition of what is essentially the same concept. Three sets of workers have thus proposed a definition independently: how do the definitions compare?

It can be said at once that they are unmistakably the same, for all three are based on the mathematical concept of "invariance." It is true that there are slight differences; and an ingenious mathematician could devise cases which would force the different definitions to give different, perhaps contradictory, answers; but these cases would be like that of the thirsty animal that drinks water containing a tasteless poison, and would be recognized intuitively as being peculiar and open to a variety of opinions. If applied to the cases that are unambiguous, the three definitions will give identical results.

At one point (§23) Sommerhoff's definition and mine seem to be incompatible, but closer study shows them to be not so; for his discussion in §32 makes clear that the "restorative forces" excluded by his definition would also be excluded by mine. The fact that his definition admits the homeostatic mechanisms to be "adapted" shows that there is no real incompatibility. On the other hand, Sommerhoff and I are by no means agreed on our vocabularies, and as any mixture of them is likely to lead to confusion I give a list of equivalences; they are not quite exact, but the table may be helpful to any worker who starts to read both publications:

* ASHBY, W. ROSS, *J. Ment. Sci.*, 1940, **86**, 478.

Idem, *Design for a Brain*. Chapman & Hall. In the Press.

ROSENBLUETH, A., WIENER, N., and BIGELOW, J., *Phil. Sci.*, 1943, **10**, 18.

<i>Sommerhoff.</i>	<i>Ashby.</i>
Closed system	: Absolute system.
State-parameter	: Variable.
Natural development	: Line of behaviour.
Focal condition	: Resting state.
Coenetic variable	: Disturbance.
Directive correlation	: Adaptation.

From these remarks the reader will gather that I strongly recommend the study of Sommerhoff's book. Though late in priority it discusses the question with a completeness that makes the earlier publications seem superficial, and it gives a definition that is much more precise than any other yet published. It gives seventy pages to the development of the definition, showing step by step why each item must be as it is. Then follows the application of the definition to the following examples :

An automatic anti-aircraft gun hitting its target.
 A hen pecking accurately at a grain of wheat.
 An insect born with protective (cryptic) coloration.
 A bird learning to discriminate between edible and inedible caterpillars.
 Muscular co-ordination.
 Vegetative homeostasis.
 Self-preserving activities.
 Regeneration and repair after injury.
 Integrated social activities.

Their wide distribution shows the breadth of the definition's applicability. The book itself is well printed and, though not easy to read, is written clearly and accurately. Only one misprint was noticed—that of Lebesgue's name on p. 107.

To sum up, the book is a valuable contribution to the study of cerebral mechanisms by the methods of physics. It shows convincingly that the rather subtle concept of "adaptation" can be given a definition that does full justice to the element of "purpose," while achieving a degree of precision and objectivity hitherto obtainable only in physics. As three sets of workers have now arrived independently at a definition from which the individuals differ only in details, we may reasonably deduce that the concept of "adaptation" *can* be so re-formulated, and that its formulation in the language of physics is now available. W. ROSS ASHBY.

Marriage and the Jewish Tradition. Edited by STANLEY R. BRAV. New York : Philosophical Library, 1951. Pp. 218.

This excellent little book is an anthology of essays by fifteen authors who are Rabbis or other learned and wise Jews.

The Gentiles, though family people, live also as nations in their own countries, but the Jews in the main have not done so.

The Jews have survived on account of their family life. One of the authors of this book states "it was the family that preserved the Jew. In my humble judgment, the greatest contribution that the Jew has made to the world, next to Ethical Monotheism, is his conception and organization of the family." Another author in this book : "The continued existence of the Jewish people is closely connected with the safeguarding of Jewish family life and with the way in which our forefathers lived."

This book should certainly be read by all educated people, who would find in it "some fulfilment of the benediction" given to Abraham, "In thee shall all the families of the earth be blessed." C. E. H. TURNER.

Vocational Rehabilitation of Psychiatric Patients. By T. A. C. RENNIE, T. BURLING and L. E. WOODWARD. New York : The Commonwealth Fund, 1950. London : Oxford University Press. Pp. 133. Price 75 cents.

The American authors of this clear and sober study "surveyed six state hospitals and one large county psychiatric hospital" to establish "the extent of need for vocational rehabilitation services."

It is observed that "rehabilitation efforts for the psychiatrically handicapped are of a pioneering nature," and that we have no "evaluation of the social and

emotional satisfactions and demands" of different jobs. The authors, however, found the prejudice against post-psychotics in industry "much less widespread and serious" than anticipated.

"Rehabilitation work is not identical with case work. It is or should be a profession in its own right. It has its own very large volume of special knowledge and its own techniques and skills." . . . "Rehabilitation 'counselling' can probably best be built upon the basic skills of the professionally trained social case worker, especially those of medical social worker and psychiatric social worker."

The rehabilitation "counsellor" integrates his work with that of the hospital occupational therapists and social workers, attends case conferences of the hospital staff, and sees the patient for the first time before discharge from hospital.

It is proposed to help the discharged patients by the provisions of the federal Vocational Rehabilitation Law.

The study is bound in paper covers.

C. E. H. TURNER.

The Story of St. Luke's Hospital. By Brigadier C. N. FRENCH, C.M.G., C.B.E. London: William Heinemann, 1951. Pp. 212. Price 8s. 6d.

The story of St. Luke's hospital is told from the time of its foundation in 1750 for the "poor and mad" until its amalgamation with the Middlesex Hospital under the National Health Act.

Brigadier French, Secretary of the hospital for several years, has given a careful balanced and detailed account of all aspects of the hospital's development.

Charles Dickens wrote in the Visitors' Book on 15 January, 1858: "Much delighted with the great improvements in the hospital under many difficulties, and with the excellent demeanour of the attendants, and with the benignant and wise spirit of the whole administration."

The book will appeal principally to those who have had a personal interest in St. Luke's Hospital.

C. E. H. TURNER.

Clinical Studies in Psychoanalysis. By SANDOR LORAND, M.D. New York: International Universities Press, Inc., 1950. Pp. 272.

This book embodies papers published at various times during the last twenty years, all of which consist of most interesting case material.

It is, however, a little difficult to judge just where the author's views may perhaps differ from orthodox psychoanalytical ones; his interpretations, while fitting the cases he so well describes, sometimes strike the reader as being far from the only possible ones, nor does he attempt to correlate them with the newer work done by those analysts who have stressed the importance of ego development.

In any case the book has this value: that it presents the psychoanalytical theme so clearly, briefly and in language so free from too much abstruse terminology that it will form a useful introduction to the reader not yet steeped in the ultra-technicalities of modern theory.

J. E. NICOLE.

Social Science and Psychotherapy for Children. By OTTO POLLAK and Collaborators. New York: Russell Sage Foundation, 1952. Pp. 242.

Here is an important and serious attempt to unite the various approaches to community living from the focal point of child guidance. The social sciences were once the basis of the social worker's *raison d'être*, but the development of psychiatry, of psychoanalysis and of child guidance gradually tended to give more and more medical flavour to social work. Hence this fascinating study of how to restore the proper sociological outlook in the consideration of the problems of child guidance.

The material on which this study is based has been collected by teams of psychiatrists, psychologists and social workers connected with child guidance, but it is to be noticed that the psychiatrists' role was that of consultants and advisers rather than therapists, the actual "treatment" being in the hands of the social workers. The whole approach to the therapeutic task was based on the fundamental conceptions of psychoanalysis.

The Foundation under the auspices of which this work has been carried out had, in addition to its therapeutic responsibilities, also assumed a teaching function in the social sciences in that it undertook the training of social workers—and a very advanced training it would appear. Arising out of this dual role, it may be hoped

that not only will the contribution of the social sciences to child psychiatry be more clearly defined, but that the data accumulated by medical psychology will not be lost to the social sciences proper.

Particularly important is the consideration given to the inter-relationships and proper fields of responsibility of the various kinds of collaborators in the teams; above all the book shows only too vividly the importance in all case-work of assessing the total situation in all its ramifications.

J. E. NICOLE.

Maternal Care and Mental Health. By JOHN BOWLBY, M.A., M.D. Geneva: World Health Organization, 1951. Pp. 179.

This very useful study consists largely of a statistical approach to the problem of mother-care (as opposed to mere mother-love), the material having been collected from sources in several countries.

In a way the conclusions reached are by no means new, but they are forcibly drawn and are based on such evidence as may help in caring for children in a manner that will support instead of contradicting the well-known platitudes about mother-care that have been repeated so often and yet been so rarely applied.

We have presented here evidence of the more subtle and delayed effects (as compared with the obvious, immediate ones) of deprivation of maternal affection, stress being laid on the ages at which such deprivation is most fraught with danger.

There are important comments on such subjects as adoption, foster families, group care and institutional care, embodying valuable reminders of our present failure to pay sufficient attention to the child's emotional needs.

J. E. NICOLE.

Personality and Psychosis. By OTHO W. S. FITZGERALD, M.A., M.D. Baillière, Tindall & Cox, 1951. Pp. 134.

In joining the ranks of characterologists, Dr. Fitzgerald approaches his problem from the angle of the psychotic personality, from which he proceeds to the delineation of prepsychotic types, in contrast to those authors who proceed from normal to abnormal. Whether yet another system of typology will help to clarify or otherwise the intricate riddle of personality remains to be seen, but this book is certainly interesting and valuably suggestive.

The author explains type formation as the interplay of inherent factors with acquired ones. The characteristics of introversion and extraversion he regards as innate, and he defines them in his own way—very different for example, from Jung's—while the acquired traits he terms the hysterical, the obsessional and the paranoid.

Where the usefulness of the author's thesis may most likely be found is in its application to prognosis and, above all, treatment. So many typologies have seemed mere academic exercises in description that any new system that is likely to have therapeutic implications is to be welcomed.

J. E. NICOLE.

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Death-rates and Causes of Death in Alcohol Addicts.

On the whole no increased mortality could be established in the material of alcoholics; the observed number of deaths does not come up to the expected number as calculated, if correction for civil status is used, but the material showed a tendency towards higher mortality figures for lower middle age, and lower values for the highest age-groups, than is the case in the material used for comparison. (Author's abstr.)

The Genetic Prognosis of Epilepsy.

Determination of the empiric genetic prognosis of epilepsy gave the following results:

Epilepsy was found to occur in 4 per cent. of the children and siblings and in 3 per cent. of the parents of cryptogenic epileptics. Oligophrenia occurred in 3 per cent. of the children and in about 1 per cent. of the siblings. The criminality among the children and siblings was one and a half times as high as that among the average population.

In symptomatic epilepsy about 1 per cent. of the siblings were affected with epilepsy and 1 per cent. with oligophrenia.

The relative fertility among patients with cryptogenic epilepsy was about 60 per cent. of the average, and was lower among males than females.

* A number of abstracts in this section are reproduced from *Chemical Abstracts*. To the Editors of this Journal we extend our grateful thanks.

The author concludes that owing to the comparatively favourable genetic prognosis, cryptogenic epilepsy does not afford a eugenic indication for induced abortion or sterilization of the patient. (Author's abstr.)

Turn-over of the Ether-soluble Plasma Phosphatides in Schizophrenia.

This study has shown an increase of the specific activity of the ether-soluble lipid P in schizophrenia, which would seem to indicate a disturbed intermediate metabolism of the ether-soluble plasma phosphatides in schizophrenia. (Author's abstr.)

Sex Steroid Therapy in Psychiatric Disorders. The Therapeutic Effect of Testosterone and Estradiol on Hospitalized Psychotics; Clinical Findings.

1. The administration of high-level, combined testosterone-estradiol therapy was followed by improvement in 23 (58 per cent.) and by convalescent status (++++ improvement) in 12 (30 per cent.) of a series of 40 hospitalized psychotics—in the main, schizophrenic, manic-depressive and involutional psychoses.

2. Improvement was attained by 74 per cent. (14 of 19) and convalescent status by 53 per cent. (10 of 19) of patients hospitalized for 6 months or less. No patient with a cumulative hospital stay in excess of 615 days for all admissions attained convalescent status.

3. Six of 7 patients (86 per cent.) of those between 16 and 25 years of age achieved convalescent status on therapy. The next responsive age category was the over 50 age-group with 4 of 17 patients (24 per cent.) attaining maximum improvement. In this series only 2 of 16 (13 per cent.) patients between the ages of 26 and 50 attained convalescent status.

4. According to pavilion of residence, the convalescent status rate was 47 per cent. (9 of 19) for reception and 14 per cent. (3 of 21) for continued treatment pavilion. The latter rate is comparable to that previously achieved in the continued treatment-assaultive pavilion with histamine biochemotherapy and in a control E.C.T. series.

5. Combined sex steroid therapy was effective in 21 per cent. (4 of 19) of patients who had previously failed to attain convalescent status with E.C.T.

6. In 7 of 8 female patients attaining convalescent status, side-effects of the sex steroid therapy were noted.

7. Utilizing the Exton-Rose two-dose procedure, a diabetic-like glucose tolerance curve was found in 7 of 10 female (70 per cent.) and 4 of 5 male (80 per cent.) patients.

8. Combined high sex steroid administration was associated with a marked increase in eosinophile counts.

9. A preliminary correlation is noted between attainment of convalescent status and of higher eosinophile levels during or after testosterone-estradiol therapy as indicated in the DEC ratio of peak post-treatment to peak pre-treatment level.

10. The lymphocyte-neutrophil ratio changes revealed that a shift towards higher ratios (indicative of relatively reduced adrenocortical activity) was found to occur following combined sex steroid therapy, with the greatest percentage change—in the authors' index of the L/N ratio percentage change—exhibited by patients attaining ++++ improvement and convalescent status. (Authors' abstr.)

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Experimental Schizophrenia-like Symptoms.

1. The effects of minute amounts of d-lysergic acid diethylamide tartrate (L.S.D.) on normal subjects, with an age range of 19-48 years, and some psychotic patients of the schizophrenic, depressive and paranoid type are reported.
2. Psychotic phenomena and alterations of the autonomic nervous system were observed. The psychotic phenomena were predominantly schizophrenia-like symptoms that were manifested in disturbances of thought and speech; changes in affect and mood; perception; production of hallucinations and delusions; depersonalization and changes in behaviour. The basic intelligence was not reduced.
3. Electroencephalographic examinations at the height of the L.S.D. reaction revealed only slight changes, principally increased alpha rhythm, except in one case where there occurred a slowing of about 2 cycles per second.
4. Rorschach tests showed abnormalities principally of the schizophrenic or paranoid type. Concrete-abstract thinking tests also, on the whole, showed responses similar to those obtained in schizophrenic patients.
5. No scientific theory for the origination of the natural psychotic phenomena or psychoses is being advanced, but the belief is expressed that experimental psychiatry progresses in the right direction. (Authors' abstr.)

Effects of Mescaline and Lysergic Acid (d-L.S.D.-25).

The effects of mescaline and lysergic acid were studied in schizophrenic patients. It was found that physiological changes were produced in these patients and that their mental symptomatology was markedly aggravated. The observations made with the above-mentioned drugs on normal individuals were compared with those seen in schizophrenic patients. Mescaline and lysergic acid are drugs that disorganize the psychic integration of a person. This disorganization is much more apparent in schizophrenics than in normals. The diagnostic, prognostic and therapeutic use of these drugs is also discussed.

(Authors' abstr.)

Effect of Drugs; Theoretical Considerations from a Psychological Viewpoint.

This paper discusses theoretical points of drug-induced abnormal mental states. The reaction of three different drugs, sodium amylal, pervitin and mescaline, on the same individual is described and the differences noted. The relationship of personality type to drug reaction is evaluated and the normalizing and disorganizing effect of certain drugs on mental patients is discussed.

(Authors' abstr.)

Mechanisms of Action of Drugs that Modify Personality Function.

An attempt has been made to examine critically what is known concerning the mechanisms through which drugs modify personality function, in terms of subjective experience, overt performance, and neurophysiology. A study of available data and the techniques

by which they have been acquired leads to several important general conclusions: (1) Not only is there a considerable degree of incommensurability between "subjective" and "objective" data, but also between data in either category that are acquired with different techniques. (2) The "organism" can never be separated from its "environment" and the two can be described only in terms of mutual interaction. (3) A "stimulus" cannot be defined in terms of its own properties alone, since its capacity to evoke responses is determined in part by antecedent events, and by particular experimental arrangements.

These conclusions can be reconciled with a monistic theory of "mind" and "body." However, it may be questioned whether concepts such as "psyche" and "soma," or their equivalents and derivatives, have not outlived their usefulness, and impede progress in psychiatry more than they foster it. An approach more consistent with the facts, which appears to be more useful in research, is one that may be called "instrumental relativity." Its salient features may be stated as follows: In psychiatry, we are concerned with the prediction and alteration of changes in the organism-environment complex at the symbolic level of functional integration. Such changes may be described in terms of various parameters, such as those of language, performance, physics and chemistry. Each group of parameters constitutes a "frame of reference" for the measurements that are made. The data so acquired may be "explained" in terms of operational constructs ("properties," "functions," "mechanisms," "theories," "laws") that are peculiar to each frame of reference. However, as the data discussed in this paper indicate, any "mechanism" (or other operational construct) in a given frame of reference can be dissociated from all other "mechanisms" in any other frame of reference, and furthermore, the rates of change of operational constructs may vary considerably in different frames of reference. It follows therefore that perfect correlations can never be made between the data acquired with one technique and those with another, although they may be related. This is true even when, because of semantic confusion, we use the same word to describe different operational constructs—e.g., stimulation, depression, inhibition, facilitation, stress, homeostasis, energy, level of integration, etc. Also, cause-and-effect relationships between successive changes in the organism-environment complex can be inferred with confidence only with respect to such changes as are described in a given frame of reference. The use of terms such as psychosomatic in a cause-effect sense is semantically unjustified and is fraught with serious sources of error.

Hence there is little justification for the despair of the neurophysiologist who felt that, as far as "mind" was concerned, the head might just as well be stuffed with cotton-wool. Although complete equivalence of what are currently termed "mental" and "material" mechanisms can never be attained, the goal of psychiatric research must be the elucidation of mechanisms, or combinations of mechanisms, in multiple frames of reference at the symbolic level of functional integration, between which correlations can be demonstrated in increasingly high degrees of probability. We must be prepared to adopt new techniques for acquiring data, and to revise our operational constructs, including dynamic formulations and classifications of psychiatric disorders, if by so doing prediction and treatment are facilitated. Such flexibility in research at non-symbolic levels has been the foundation for progress in other medical fields, and promises also to have great value for psychiatry.

(Author's abstr.)

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- *Results of Treatment of Schizophrenia in a State Hospital. *Currier, G. E., et al.* 80

Dynamic Concepts of Migraine; A Character Study of One Hundred Patients.

The character patterns of 65 women and 35 men with migraine were studied according to the principles of the psychoanalytic concepts of character formation. The persons of the group consistently possessed traits that indicated a marked narcissism, as well as a strongly developed aggressive instinct. Lack of demonstration of affection or strictness of training by the parents frustrated these needs, resulting in ambivalences and the development of an ultramoral and rigid superego. In all the patients the migraine attack began when hostilities accumulated beyond the individual's capacity for tolerance of frustration. Migraine is considered a vegetative neurosis, the physiologic vasomotor manifestation of suppressed or repressed hostility initially directed specifically toward the family and later to frustrations in general. (Author's abstr.)

Fatalities in Insulin Therapy of the Psychoses; Analysis of Eight Cases.

Eight fatal cases of insulin therapy in psychiatric practice are presented. Factors which may contribute to the fatal outcome are discussed.

The following considerations may be of value in anticipating adverse reactions: (1) a history of such atypical responsivity to medication as respiratory collapse or syncope; (2) factors adversely affecting the physiological systems regulating insulin-glucose relationships, such as malnutrition, avitaminosis, use of certain drugs, autonomic imbalance, and excessive fear of treatment; (3) undue resistiveness to insulin as manifested by high dose requirements or the occurrence of relatively few comas. This may be accompanied by overactivity of the sympathetic nervous system, excessive fear of treatment, and a tendency to sudden cardiorespiratory complications; (4) undue sensitivity to insulin as manifested by (a) low or rapidly decreasing dose requirements; (b) unusually deep coma; (c) difficulty in termination of coma; (d) a tendency to "after-shock," and (e) probably, the presence of low vital signs. (Authors' abstr.)

Changes in Phosphatase Activity of Serum and Urine after Shock Therapy.

Alkaline and acid phosphatase activities of serum and acid phosphatase activity of urine all are in the normal range in patients with schizophrenic, manic-depressive, or involutional psychoses, or with severe neuroses; serum acid phosphatase activity appears to be low in the normal range.

Single electroshock treatments do not affect serum alkaline or acid phosphatase activities. A course of electroshock or ambulatory insulin treatment commonly results in lowering of phosphatase activities. (Authors' abstr.)

Blood Glutathione Level in Mental Disease Before and After Treatment.

The blood glutathione level is in or below the lower normal range in untreated patients with manic-depressive, involutional or schizophrenic psychoses; some patients with severe neurosis show the same change.

After courses of electroshock or ambulatory insulin treatments that result in improvement, the blood glutathione level rises to, or toward, the normal if initially low ; little or no change occurs if the initial concentration of blood glutathione is not low.
(Authors' abstr.)

Results of Treatment of Schizophrenia in a State Hospital ; Changing Trends since Advent of Electroshock Therapy.

The results of treatment in 112 female schizophrenic patients admitted during the year 1 July, 1946, to 30 June, 1947, were compared, after a follow-up period of 13 months to 3 years, with the results in 119 female patients admitted during 1934 and 1935. Of the 112 patients admitted in 1946-1947, 75 received one or more courses of electroconvulsive therapy.

The over-all results were significantly better in the 1946-1947 period, 60 per cent. of the patients being improved or much improved, as compared with 22.5 per cent. of the patients admitted during 1934 and 1935. This difference was due to superior results obtained in those members of the 1946-1947 group who received electroshock therapy ; 75 per cent. of these patients were improved or much improved, as compared with 30 per cent. of the untreated patients in the same series.

A study was made of the following variables which were found to influence the outcome significantly : subtype of schizophrenia, age on admission, type of onset and duration of illness prior to hospitalization. Also, cases were matched from the two periods under review in order to determine whether or not a combination of the foregoing factors might be responsible for the differences in the results of treatment.

An analysis of the data suggested that the more successful results observed in the group receiving electro-shock therapy were due in large part to the shock treatment itself, but contributing to its success was a preponderance of favourable prognostic factors which were present in the members of this group.

The observations suggested that in the past 10 or 15 years the community has become more aware of the importance of early hospitalization and treatment for schizophrenic patients.
(Authors' abstr.)

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Intraventricular Medication in Catatonic Stupor (Preliminary Communication).

Some of the available evidence for the nature of the disorder underlying catatonic stupor is discussed and arguments are presented for the clinical trials carried out.

The clinical effects of injections of each of four drugs into the lateral cerebral ventricles in cases of schizophrenia are described. The drugs used were: (1) cholinesterase, (2) procaine, (3) pentamethonium iodide, and (4) flaxedil.

Three cases were treated. In the first case all four drugs were used; in the second case cholinesterase, pentamethonium iodide and flaxedil. The effect aimed at was to relieve the condition of catatonic stupor. This effect was achieved to a varying extent in all three cases, and was most marked with cholinesterase in Case 1, and pentamethonium iodide in the three cases. (Author's abstr.)

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Theta and Beta Rhythm in the Electroencephalograms of Normal Adults.

1. Low voltage theta activity was detected in 64 per cent. of a group of 161 young normal adults and in 24 per cent. of 50 mentally normal seniles, the difference between the two groups being significant at the 1 per cent. level. This decrease of theta incidence with increasing age was discussed in relation to maturation processes. Evidence was further presented to indicate that theta activity in the senile group represented a different phenomenon from that encountered in the younger group.

2. Variations in theta activity during either visual and/or mental tasks or during slight changes in temper were observed in 26 per cent. of the subjects showing theta rhythm in the younger group. Two classes of activity were differentiated, those harmonically related to alpha frequencies and those not. Observations on theta variation appeared to accord with Walter's findings in respect of theta rhythm and emotional level. Incidence of theta rhythm was significantly greater among females than males.

3. Low voltage beta activity was observed in 53 per cent. of the younger group and 62 per cent. of the senile group, the difference not being significant. Amplitudes were significantly greater in the older group however.

4. Fifty-one per cent. of those with beta activity in the younger group showed variation of beta rhythm with either visual and/or mental activation. Evidence was presented to suggest that beta activity may in part at least represent accelerated rhythms resultant on scansion of cortical projection and association areas. A highly significant relationship between beta incidence and alpha type was found to support this hypothesis, although the study needs repetition with the aid of automatic frequency analysis before certainty can be established.

5. A significantly greater incidence of beta activity was found in the females as compared with the males of the younger group, whilst in the senile group a significantly greater incidence was found in a group of Europeans as compared with a group of Africans. These findings were briefly discussed in relation to cultural influences on the E.E.G.

(Author's abstr.)

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Nonconvulsive Electrostimulation and the Pituitary-Adrenocortical System.

- (1) Eosinophil counts were done on 25 non-fasting patients in a state mental hospital. The initial counts ranged from 34 to 640, 81 per cent. being in the range of 60 to 250.
- (2) Electrostimulation with and without pentothal anesthesia produced a marked eosinopenia, generally three hours after treatment.
- (3) After pentothal anesthesia alone, a slight transient drop of eosinophils was observed.
- (4) Controls showed no consistent drop.
- (5) Nonspecific stress was eliminated as cause of the eosinopenia.
- (6) It is assumed that the electric current stimulates the pituitary-adrenocortical system by direct action on the hypothalamic area.
- (Authors' abstr.)

Homeostatic Studies in Patients with So-called Psychosomatic Disease (Peptic Ulcer).

Forty male patients with a so-called psychosomatic disorder, peptic ulcer, were investigated from the standpoint of the efficiency of their autonomic regulatory apparatus by means of the cold pressor test. The responses of the patients to this test differed signifi-

cantly from those found in normal patients and two distinct groups of hyper-reactors and hyporeactors could be distinguished. It is suggested that the symptomatology in the so-called psychosomatic disorders may result from a disturbed autonomic regulatory mechanism as well as from the impact of abnormal personality and emotional constellations.

For determining the presence of actual fluctuations during the period of investigation beyond those due to chance, the formula for analysis of variance as described by Snedecor was used. The difference between the means of two single months or seasons was compared by the "t" test.

(Authors' abstr.)

Changes in Nervous Tissues and Study of Living Organisms in Mental Disease.

Abnormal changes in cytochemical processes in nerve-cells occur as a constant feature of dementia praecox. Seventy biopsies are reported. The metabolic disturbances caused by inclusion bodies are exhibited prominently by the nucleus and cytoplasm.

(1) An early stage involves the presence of inclusion bodies in the cytoplasm with increase of deoxyribonucleic acids in the nucleus.

(2) This continues into a stage in which the nucleus becomes inflated with a great quantity of nuclear sap. The cytoplasm is stretched, and impoverished in Nissl substance.

(3) Naked nuclei occur in profusion when the cytoplasm breaks away from the nucleus. These are the outstanding changes in dementia praecox.

(4) Pycnosis is another change affecting fewer cells, usually those closer to the surface of the cortex. The linin reticulum of the nucleus develops into a dense network (possibly histone) gradually excluding the nuclear sap, until the nucleus becomes homogeneous and shrunken. The cytoplasm shrinks and loses its capacity for repair, but retains its cytochrome and probably respiration.

(5) Collagen-like changes in some cases affect the pycnotic nuclei. This substance oozes out into the cytoplasm as droplets. The glia and vascular tissues also show an increase of collagen.

(6) Neurofibrillar damage is usual. The neurofibrils in the nerve-cells are congealed or destroyed in the region of cytoplasm occupied by inclusion bodies. The axons of radial bundles show distortions of calibre.

(7) Gliosis is another feature of abnormal metabolism. It is shown by growth of sclerosing fibers around astroglia cells in the cortex, and by proliferation of oligoglia nuclei and sclerosing fibres in the white matter.

(8) Proliferation of mesoglia and microglia nuclei around blood-vessels is a common feature. The entire configuration of changes is consistent in most cases.

(9) The presence of a pelomorphie organism is described as a causal factor common to all these changes; and this has been demonstrated by the use of dark phase microscopy which shows the vital activities of the organism.

(Authors' abstr.)

Thought Processes as Related to Brain Metabolism in Certain Abnormal Conditions.

1. Any defect in the biochemical processes of the brain, especially those concerned with energy transformation, may make itself known by alterations in cerebral function, including personality changes which may be neurotic or psychotic in character.

2. Our most secure metabolic evidence is observed in association with a failure in the first level concerned with the mobilization of energy; namely, the oxidation of glucose, and may be seen in the clinical changes of hypoglycemia, anoxia or avitaminosis.

3. The second level involves a faulty storage of energy in the energy-rich phosphate bonds, so that the energy made available by oxidation cannot be applied to useful purposes but is merely dissipated as heat. Such a defect may be a factor in the production of narcosis.

4. Even if cerebral function is adequately supported, mentation may nevertheless be warped at a still higher level; for example the synthesis of acetylcholine may proceed normally, at the expense of energy from phosphate bonds, but the physiological effects of that neurohormone may be blocked by atropine and with excessive doses of that drug delirium may ensue.

5. The production of psychotic reactions with ACTH and cortisone invites further study. These hormones disturb enzymatic reactions by altering the electrolyte and water patterns of the body, thus changing the physico-chemical environment in which the various enzymes must operate. It is also possible that cortisone may affect cerebral enzymatic processes directly. In any event the total energy exchange of the brain as measured by cerebral metabolic rate does not seem to be altered by ACTH or cortisone.

6. The structural changes in the brain associated with some psychoses afford a beachhead for further attack.

7. Finally it must be admitted that the so-called "functional" psychoses have hitherto resisted all efforts to disclose convincing organic clues. But with the observation that minute amounts of psychochemical agents may evoke a temporary psychosis, it seems possible to determine whether or not these psychoses are also results of a faulty biochemistry.

(Author's abstr.)

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Life Situations, Emotions and Neurocirculatory Asthenia. (Anxiety Neurosis, Neurasthenia, Effort Syndrome.)

1. Neurocirculatory asthenia (anxiety neurosis, neurasthenia, effort syndrome) is a chronic disorder which runs in families. It is probably a fairly common disorder.

2. Various names have been used for the disorder.

3. The cause of the disorder is unknown.

4. The symptoms of patients, according to their stories, are brought on by muscular work, other sicknesses, emotion-provoking situations, pregnancy, heat and cold, military service, and no obvious factors. The truth of such correlations has never been verified adequately by anyone.

5. Quantitative and objective abnormalities have been demonstrated, in response to various stimuli and stresses, in patients' pulses, minute respiratory volumes, ventilatory efficiency, blood lactate concentration, work performances, oxygen consumptions, wincing and withdrawal reactions, among others.

6. Stimuli and stresses which produce abnormalities of responses or unusual responses at lower stimulus levels include: pain, cold, muscular effort, carbon dioxide, noise, flash, and "anticipation."

7. These experiments give no crucial or final evidence as to the cause of the disorder or its relationship to more complicated or natural life situations.

8. The twenty-four hour amount of urinary excretion of 17-ketosteroids was the same in patients as it was in comparable control subjects. Since this has been considered by some to be an "index of stress," this finding suggests either that excretion of 17-ketosteroids is not a reliable or complete indicator of "stress," or that the disorder does not call forth the same "stress mechanisms" as do some other illnesses.

9. A crucial causal relationship of this disorder to life situations and emotion-provoking situations has neither been proven nor disproven.

10. No techniques have been developed as yet for use in this field which permit conclusive observations concerning the exact relationships, if any, of life situations and emotion-provoking situations to this disorder, or which allow for a definite statement as to whether an illness is or is not on a "psychogenic" basis.

11. This disorder does not lead to a high mortality rate.

12. Although these patients had "anxiety" as a characteristic phenomenon, they did not develop, as judged by a twenty-year follow-up study, to any unusual extent diseases such as hypertension, peptic ulcer, asthma, ulcerative colitis or thyrotoxicosis, which some authors have speculated are caused by "anxiety."

13. As judged by published therapeutic results, patients with this disorder do as well with simple reassurance and the passage of time as do apparently similar cases managed by prolonged psychotherapy, psychoanalysis, electric convulsion procedure, ergotamine tartrate and adrenal denervation.

14. The cause and specific treatment of this disorder are as yet unknown.

(Authors' abstr.)

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A New Adjuvant in Postalcoholic Psychomotor Agitation.

A definite need exists for a drug to relieve the symptom of psychomotor agitation frequently observed in alcoholic patients in the period of recovery after a bout of intoxication.

Dimethylane (2,2-diisopropyl-4-hydroxymethyl-1, 3-dioxolane) has been shown to reduce markedly the time required for control of this symptom. The drug provoked no toxic effects in the therapeutic dosages administered.

(Authors' abstr.)

The Occupational Performance of Thirty Alcoholic Men.

The findings of this study indicate a wide range of occupational behavior among the 30 alcoholic patients interviewed, but a preponderance of certain common traits.

The common traits observed in this group of patients were: (1) a capacity to visualize vocational goals along with incapacity for sustained effort in vocational performance; (2) a preference for work experiences that entail creative energy, independence, contact with the public, excitement and movement; and (3) frequent changes in employment that, for the most part, could be attributed to restlessness and inebriety.

The small size of the sample and the mode of its selection preclude the generalization of the findings of this study to the total male alcoholic population or to any well-defined segment of it. It is interesting to note, however, that the common traits in occupational behavior of these alcoholic patients, aside from being traceable in part directly to the problems created by their drinking, seem to reflect underlying emotional patterns of tension and need for release which have been postulated as characteristic of the personality of alcoholics.

(Author's abstr.)

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1. Biochemistry, Pathology, etc.

Changes in Acetylcholine Content of the Brain during Exposure to Cold. Milch, Lawrence J., Midkiff, Harney F., Matthews, Priscilla, and Chinn, Herman I. (Air Force School of Aviation Med., Randolph Field, Texas). [*Proc. Soc. Exptl. Biol. Med.*, **77**, 659-61 (1951).]

Adult male rats were exposed to a temperature of -12° for 2 hours. The average body temperature decreased to 15° but none died from the cold. The free and total acetylcholine concentrations of the brain tissue were significantly increased by the treatment. L. E. GILSON (Chem. Abstr.).

The Role of Acetylcholine in the Central Nervous System. Feldberg, W. (Natl. Inst. for Med. Research, London). [*Brit. Med. Bull.*, **6**, 312-21 (1950).]

The role of acetylcholine (I) as a central synaptic transmitter is reviewed. There are many observations which can be accounted for conveniently and satisfactorily only by the (I) theory even though (I) is probably not the universal central synaptic transmitter. A. DIETZ (Chem. Abstr.).

Preparation of Soluble Cholinesterases from Mammalian Heart and Brain. Ord, Margery G., and Thompson, R. H. S. (Guy's Hosp. Med. School, London). [*Biochem. J.*, **49**, 191-9 (1951).]

Rat heart has been chosen as the source of pseudocholinesterase (splits actively benzoylcholine) and rat brain for true cholinesterase. The former enzyme preparation was purified 30 times, the latter 10 times. The heart preparation was found to consist largely of an unknown esterase which differs from both the true or pseudocholinesterase. The heart cholinesterase active against benzoylcholine is not affected by brief tryptic digestion but the brain cholinesterase is inactivated. Various surface-active agents were used to bring the brain cholinesterase into solution. The solubilizing effect is probably due to their action on lipoprotein complexes containing the cholinesterase. It is suggested that perhaps the brain cholinesterase is a lipoprotein. S. MOGULIS (Chem. Abstr.).

The Urea Nitrogen Content of the Cerebrospinal Fluid. Lickint, Fritz (Stadtkrankenhaus, Dresden-Neustadt, Ger.). [*Arch. Psychiat. Nervenkrankh.*, **186**, 194-7 (1951).]

In 23 almost normal persons the urea N concentration in cerebrospinal fluid (C.S.F.) ranged from 7.4 to 16 mgm. per 100 ml. These values were 71 to 90 per cent. of the corresponding concentrations in blood serum. Urea N was determined in C.S.F. in 172 diseased persons. In brain concussion, neurosyphilis, encephalitis, epilepsy and eclampsia most of the concentrations were normal, in hydrocephalus most were low; in meningitis and kidney disease large increases were found. The residual N (I) concentration of C.S.F. varied with the urea N concentration.

The Residual Nitrogen of Cerebrospinal Fluid (with Particular Attention to its Relation to Other Nitrogen-containing Constituents). [*Ibid.*, 198-203.]

In 13 normal subjects the (I) concentration of C.S.F. ranged from 12 to 19 mgm. per 100 ml. and was about 42 per cent. below the corresponding concentration in the blood serum. (I) was determined in 139 diseased persons. In hydrocephalus, brain concussion, encephalitis, eclampsia and neurosyphilis most of the concentrations were normal; in meningitis both normal and high concentrations were found; in kidney disease large increases occurred. The determination of creatinine, uric acid, amino acids, xanthoprotein or indican cannot be substituted for determination of (I) because these substances vary independently. WARREN M. SPERRY (Chem. Abstr.).

Shifting of Cations in the Cerebrospinal Fluid as a Cause of Pruritus. Koenigstein, Hans (Hebrew Univ., Jerusalem). [*J. Investigative Dermatol.*, **17**, 99-123 (1951).]

Cisternal injection of 1-2 mgm. of KCl into cats or rabbits produces scratching attacks, and the severity of the attack parallels the concentration of K ion. The effect is accompanied by an approximate doubling of the concentration of K ion in the cerebrospinal fluid. Injection of morphine, picrotoxin, NH_4Cl , pilocarpine or caffeine in sufficient quantities to produce scratching attacks is in 60 per cent. of the cases accompanied by a rise (sometimes of more than 100 per cent.) in K ion content of the cerebrospinal fluid; the increase in the blood serum is much less and appears at a slower rate. Cations resembling K ion are, except for Na ion, likewise pruriginous in effect. Addition of small amounts

of oxalates, phosphates or citrates to the cerebrospinal fluid likewise produces scratching attacks or cramps; these reduce Ca ion concentration in the fluid. Re-establishment of the normal Ca/K ion ratio is effective in alleviating the attack caused by an excess of K ion; Mg ions can be injected subcutaneously in place of Ca ion.

P. Y. JACKSON (Chem. Abstr.).

Colorimetric Determination of Acetone Bodies in the Cerebrospinal Fluid. Kodama, Takashi, Kanno, Saburo, Muto, Nobuo, Kawamura, Taro, and Hoshino, Shigetsugu (Kanagawa Prefectural Public Health Lab., Yokohama). [*Igaku to Seibutsugaku (Med. and Biol.)*, **19**, 1-3 (1951).]

Place 1 c.c. of the cerebrospinal fluid in a small test-tube, dissolve 2 granules of solid KOH (average weight of 0.138 gm. per granule) with shaking, add 1 drop of salicylaldehyde from a buret, and heat on a micro burner just to boiling. After 0.5-1.5 hrs. compare the colour of the reaction mixtures with those of the controls, which are prepared in the same manner using serial dilutions of purified acetone (treatment with KMnO_4 , dehydration with K_2CO_3 , and distillation) (0.25-32 mgm./100 c.c.). The cerebrospinal fluid to be used in this determination is best prepared on the day of the experiment, but when it is impossible to carry out the determination on that day it can be preserved in the cold (or at room temperature, when an ice box is not available) after adding 1 drop of 5 per cent. HCl to 1 c.c. of the sample. This reaction is positive with acetone and with acetoacetic acid, but is negative with β -hydroxybutyric acid. MICHINORI NAKAMURA (Chem. Abstr.).

Cerebrospinal Fluid Changes in Toxicosis Due to Infantile Diarrhoea. Choremis, C., Konstandinides, B., Kiza, M., Markidou, A., and Nestoridou, M. (Athens Univ., Greece). [*Ann. Paediat.*, **177**, 77-83 (1951).]

Cerebrospinal fluid (I) changes in toxicosis resulted from blood biochemical changes. The amount of (I) was reduced. The sugar concentration was elevated, that of chlorides and K decreased. Alkali reserve was always reduced, following the decrease of the blood alkali reserve; the decrease was attributed to the low blood Na.

BARBARA R. MURRAY (Chem. Abstr.).

The Appearance of Uric Acid in the Cerebrospinal Fluid of an Infant with Toxic Gastro-enteritis. Ferenz, P., and Boda, D. (State Infants' and Children's Hosp., Pestszentlőrinc, Hung.). [*Ann. Paediat.*, **175**, 459-73 (in German).]

The cerebrospinal fluid of these children showed an accelerated reduction of KMnO_4 caused by an increased uric acid content. The total protein and number of cells were within normal limits.

BARBARA R. MURRAY (Chem. Abstr.).

Salt-wasting Syndrome Associated with Cerebral Disease. Peters, John P., Welt, L. G., Sims, E. A. H., Orloff, J., and Needham, J. (Yale Univ.). [*Trans. Assoc. Am. Physicians*, **63**, 57-64 (1950).]

An extra-pituitary cerebral structure may be involved in the normal metabolism of Na. Salt depletion in patients with diseases of the central nervous system is of clinical importance.

JOSEPH S. HEPBURN (Chem. Abstr.).

Action of Aneurine on Muscle Fatigue. Lissák, K., Martin, J., and Ángyán, A. (Univ. Pécs, Hung.). [*Z. Vitamin-Hormon- u. Fermentforsch.*, **3**, 487-93 (1950) (in English); cf. *C.A.*, **33**, 8761²; **37**, 3478⁵.]

Contrary to the findings of others (Chauchard, *C.A.*, **36**, 2594^{5 6}; Briem, *C.A.*, **35**, 775¹), the authors showed that intravenously injected aneurine causes transitory acceleration of muscle fatigue and fails to prevent Wallerian degeneration in Sherrington nerve muscle preparations of cat gastrocnemius. Aneurine does not sensitize the muscle to acetylcholine.

E. HIRSCHBERG (Chem. Abstr.).

Effect of Nutrition on the Distribution of Vitamin B₁ in Parts of the Nervous System. Zaprudskaya, D. S. (Pedagog. Inst., Rostov). [*Biokhimiya*, **16**, 280-5 (1951).]

The amount of thiamine (I) was determined in the various parts of the nervous system of rabbits (newborn, 10, 35, 75, 120 days, and grown-up) and cats (60 days and grown-up) which had been raised on a normal diet and on a diet containing added 50γ (1 kgm.). No increase of (I) was observed in the nerve tissues of growing rabbits saturated with (I), as compared to the controls. A slight increase was detected in adult rabbits. (I) increased considerably in the nerve tissue of cats which had received additional (I) in their food. The amount of (I) in the nerve tissues of the control rabbits of various ages was greater than that found in the same nerve tissues of the control cats. H. P. (Chem. Abstr.).

Aneurine Content of the Nerves of B₁-avitaminotic and Normal Rats. Martin, Catherine and Lissák, K. (Univ. Pécs, Hung.). [*Z. Vitamin-, Hormon- u. Fermentforsch.*, **3**, 494-6 (1950) (in English).]

Young rats were maintained on an aneurine-deficient diet until severe deficiency symptoms were observed. The following aneurine values (γ /gm. nerve tissue) were obtained by the thiochrome procedure: normal brain, 0.56; B₁-avitaminotic brain, 0.11 normal sciatic nerve, 0.127; B₁-avitaminotic sciatic nerve, 0.056.

ERICH HIRSCHBERG (Chem. Abstr.).

Cholesterol Content of Tabetic Spinal Cord. Dixon, K. C., and Herbertson, B. M. (Univ. Cambridge, Engl.). [*J. Path. Bact.*, **63**, 491-7 (1951).]

Samples of the posterior columns of 7 tabetic spinal cords contained less than half the cholesterol found in similar samples from 4 normal cords. The amounts of cholesterol in both posterior and lateral columns of 16 normal spinal cords were determined and showed an average ratio of 1.035. In 8 tabetic cords the ratio averaged 0.55.

JOHN T. MYERS (Chem. Abstr.).

Distribution of Radioactive Phosphorus in Normal and Diseased Brain Tissue; Experimental and Clinical Observations. Stern, W. Eugene, and Marshall, Curtis (Johns Hopkins Univ., Baltimore, Md.). [*Proc. Soc. Exptl. Biol. Med.*, **78**, 16-20 (1951); cf. C. A., **45**, 10378f.].

L. E. GILSON (Chem. Abstr.).

Brain Metabolism and Activity. McIlwain, H. (Maudsley Hosp., London). [*Brit. Med. Bull.*, **6**, 301-4 (1950).]

The changes in blood during passage through the brain, the changes in brain constituents and the metabolic activities of the brain tissue are reviewed.

A. DIETZ (Chem. Abstr.).

Conduction of the Nervous Impulse: Some Recent Experiments. Hodgkin, A. L. (Physiol. Lab., Cambridge, Engl.). [*Brit. Med. Bull.*, **6**, 322-5 (1950).]

The basis of the action potential and the effects of Na and chloride ions are reviewed.

A. DIETZ (Chem. Abstr.).

2. Pharmacology and Treatment.

Pharmacological Aspects of Drugs of Extrapyrarnidal Action. II Antihistamines, neuromuscular Antispasmodics, Sympathomimetic Amines. Holz, S. (Univ. Central Venezuela). [*Acta cient. venezolana*, **2**, 17-23 (1951); cf. C. A., **45**, 6300g.].

ERICH HIRSCHBERG (Chem. Abstr.).

Cerebral Effects of Pentothal Sodium in the Toxemias of Pregnancy. Taylor H. Winfield, and McCall, Milton L. (Philadelphia General Hosp., Philadelphia, Pa.). [*J. Phila. Gen. Hosp.*, **2**, 86-9 (1951).]

Slow intravenous administration of 0.2-0.9 gm. pentothal-Na as 2.5 per cent. solution to toxemic pregnant women depressed cerebral metabolic rate 21, increased cerebral vascular resistance 11, lowered mean arterial blood pressure 3, depressed cerebral blood flow 16 per cent.

JOSEPH S. HEPBURN (Chem. Abstr.).

Actions of Nicotine on Spinal Reflexes. Nicolau, J. del Castillo. [*Arch. inst. farmacol. exptl. med. (Madrid)*, **2**, 179-90 (1950).]

In decerebrate or anesthetized cats, the actions of nicotine (I) can be divided into an initial period in which the effects depend directly on the concentration of (I) in the blood, and a second period due to (I) reaching the central nervous system or to lasting changes produced during the first period. The flexor reflex is increased 40 per cent. during the first period. Rotation is inhibited, and finally disappears during the first period, then recovers, and is depressed again during the second period. The crossed extensor reflex is depressed during the first period, and increased up to 50 per cent. during the second period. The tonus of skeletal muscle is depressed during the first and augmented during the second period. Quantitative relationships between the effects of (I) on rotation and on crossed extension suggest an intimate relation between the mechanisms for these reflexes. Antagonism between (I) and procaine can be demonstrated with the flexor, but not with the extensor reflex.

MARSHALL E. DEUTSCH (Chem. Abstr.).

Changes in the White Cells and Sugar of the Blood as a Result of Electronarcosis. Geiser, Max (State Health Inst., Münsingen, Switz.). [*Monatsschr. Psychiat. Neurol.*, **122** 47-66 (1951).]

In 13 schizophrenic patients the blood-sugar concentration rose during and after electronarcosis to an average maximum 47 per cent. above the control level at 5 minutes after the end of the narcosis, and fell to the starting concentration within 1 hour.

WARREN M. SPERRY (Chem. Abstr.).

Central and Peripheral Nervous Excitability in Mammals Before and After Prostigmine. Cicardo, V. H., and Bremier, R. (Hosp. Tornú, Buenos Aires). [*Rev. soc. argentina biol.*, **26**, 318-25 (1950); *Comp. rend. soc. biol.*, **145**, 590 (1951).]

Rheobase and chronaxia determinations on guinea-pigs before and after prostigmine injections (even up to lethal doses) showed no changes. The excitability of the central nervous system (pyramidal bundle in guinea-pigs, cortical motor centres in dogs) was not altered by prostigmine. This does not support the hypothesis of intervention of acetylcholine in neuromuscular transmission and synapses of the central nervous system.

L. E. GILSON (Chem. Abstr.).

Intoxication Tests for Drinking Drivers and Pedestrians. Hunter, Oscar B., Jr. (1835 I St., N.W., Washington, D.C.). [*Trans. Am. Therap. Soc.*, **41**, 27-30 (1941) (pub. 1942).]

The applicability of various chemical tests is discussed. W. C. TOBIE (Chem. Abstr.).

Anticonvulsant Action of Ergotamine. Riechert, Willi (Univ. Heidelberg, Ger.). [*Arch expthl. Path. Pharmacol.*, **213**, 82-7 (1951).]

Intramuscular injection of 5 mgm./kgm. ergotamine (I) or 1 mgm./kgm. dihydroergotamine (II) into white rats prevented convulsions elicited with intravenous administration of 20-25 mgm./kgm. cocaine. (I) also prevented convulsions produced with cocaine and pontocaine and markedly reduced intensity and duration of convulsions produced with metrazole, coramine, picrotoxin and hexeton. (I) and (II) prevented the lethal action of 20-25 mgm./kgm. triphenyltetrazoline chloride, apparently by preventing the compound from entering the brain. The anticonvulsant actions described may be due to a similar mechanism.

KARL F. URBACH (Chem. Abstr.).

Metabolism and Glutamic Acid Content of Rat Brain in Relation to Thiopentone Anesthesia. Dawson, R. M. C. (Whitchurch Hosp., Cardiff, Engl.). [*Biochem. J.*, **49**, 138-44 (1951).]

Thiopentone anesthesia reduces the free glutamic acid content of the rat brain which may be partly accounted for by the small increase in glutamine. The oxidation of minced brain tissue is decreased by low concentration of thiopentone, which also reduces the level of free ammonia in the brain. Glutaminase is unaffected but adenylic deaminase is somewhat inhibited by the thiopentone.

S. MORGULIS (Chem. Abstr.).

Chronic Epilepsy in the Monkey Following Multiple Intracerebral Injections of Alumina Cream. Chusid, Joseph G., Pacella, Bernard L., Kopeloff, Lenore M., and Kopeloff, Nicholas (Psychiatric Inst., New York, N.Y.). [*Proc. Soc. Exptl. Biol. Med.*, **78**, 53-4 (1951).]

L. E. GILSON (Chem. Abstr.).

Mechanism of Electroshock Therapy. Cerebrospinal Fluid Studies. Spiegel-Adolf, M., Wilcox, Paul H., and Spiegel, E. A. (Temple Univ., Philadelphia, Pa.). [*Trans. Am. Therap. Soc.*, **48**, 160-1 (1947) (pub. 1950); cf. *C.A.*, **43**, 5468b.].

In cerebrospinal fluid the mean extinction coefficient at 2650A (usually attributed to ascorbic acid) was 1.99 in untreated schizophrenics and 1.24 in controls. Increases in lipolytic activity and other enzymes after electroshock are discussed.

W. C. TOBIE (Chem. Abstr.).

Comparative Actions of Analgesic, Hypnotic and Paralytic Agents on Hindlimb Reflexes in Chronic Spinal Dogs. Houde, Raymond W., Wikler, Abraham, and Irwin, Samuel (U.S. Public Health Service Hosp., Lexington, Ky.). [*J. Pharmacol. Exptl. Therap.*, **103**, 243-8 (1951).]

Characteristic changes in the pattern of the hindlimb reflexes observed after administration of potent analgesic (morphine and methadone), hypnotic (thiopental and pentobarbital) and paralytic (mephenesin and benzimidazole) agents are described. The specificity of the changes of the pattern may serve as a basis for classifying new compounds. The proper place of studies on spinal animals in research on the mechanism of drug action is discussed.

L. E. GILSON (Chem. Abstr.).

Toxic Reactions on the Labyrinthine Reflexes Caused by Tetraethylthiuram Disulfide. Brug, J., and Funcke, A. B. H. (Univ. Utrecht, Netherlands). [*Arch. intern. pharmacodynamie*, **87**, 113-17 (1951).]

Guinea-pigs surviving a single (1-2 gm.) or several daily oral doses of tetraethylthiuram disulfide lose static labyrinthine reflexes after some weeks. The cause of the symptoms has not yet been determined.

M. L. C. BERNHEIM (Chem. Abstr.).

Effect of Hypercapnia and Hypoxia on Electrically Induced Convulsions in Rabbits. Dahlberg-Parrow, Ragna (Univ. Uppsala, Sweden). [*Acta Physiol. Scand.*, **23**, 55-63 (1951).]

It was shown in basic experiments on epileptics that decreasing the CO_2 concentration in the blood induced a convulsive seizure while administration of excess CO_2 stopped it. Epileptic seizures could also be induced by decreasing the O_2 content of inspired air or by lowering the CO_2 tension of the blood. In unanaesthetized and uncurarized rabbits convulsions were induced electrically. The course of the convulsions was followed by observing the activity of the gastrocnemius muscles electromyographically. Hypercapnia was produced by breathing a mixture of 12 per cent. CO_2 in O_2 for 5 minutes, while hypoxia was produced by breathing pure N_2 for 10 seconds. Hypercapnia caused a prolongation of the flexion and shortening of the extension of the tonic phase. On the contrary the clonic phase was absent in most animals. In the latter the seizures were shortened by hypoxia to a particularly marked degree.

S. MORGULIS (Chem. Abstr.).
